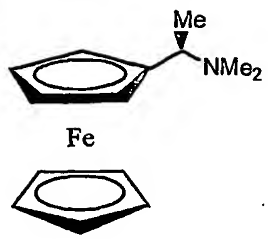
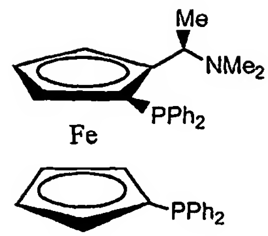
PROCESS FOR THE PRODUCTION OF ASYMMETRIC TRANSFORMATION CATALYSTS

This invention relates to a novel process for the production of asymmetric transformation catalysts, in particular to such a process for the production of phosphine and arsine ligands having a chiral centre at phosphorus, or arsenic as the case may be. Such ligands are found to be useful in a wide variety of asymmetric transformation reactions, including hydrogenation and carbon-oxygen and carbon-nitrogen bond formation reactions. The process of the invention may be applicable to the production of chiral catalysts containing aromatic ring systems generally, and is especially useful in the production of metallocene-based phosphine and arsine ligands. The invention also relates to chiral catalysts produced by the process of the invention, and to the use of such catalysts in asymmetric transformation reactions.

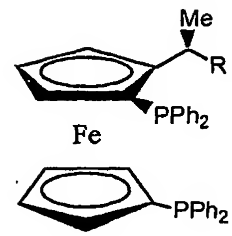
Ferrocene as a backbone for diphosphine ligands was introduced by Kumada and Hayashi based on the pioneering work of Ugi related to the synthesis of enantiopure substituted metallocenes[1]. A number of these ligands are shown below:



Ugi's Amine



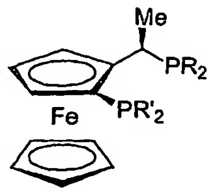
PPFA



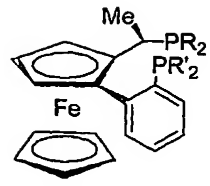
R = Me_2N, BPPFA
R = OH, BPPFOH

Ppfa as well as bppfa and bppfoh proved to be effective ligands for the catalysis of a variety of asymmetric transformations. From this starting point, many chiral ferrocene-based bisphosphine ligands with a range of structural variation have been developed in the last few years.

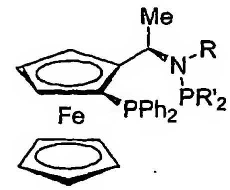
Certain types of known ligands exhibit both planar and carbon chirality:



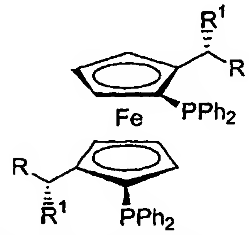
Josiphos: R = Cy, R' = Ph
PPF-tBu$_2$: R = t-Bu, R' = Ph
Xyliphos: R = 3,5-Me$_2$Ph, R' = Ph
cy$_2$PF-Pcy$_2$: R = R' = Cy



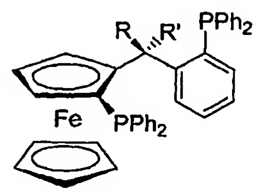
Walphos



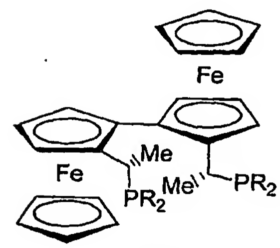
BoPhoz



Mandyphos (FERRIPHOS)



Taniaphos
1a: R = H, R' = NMe$_2$
1b: R = OMe, R' = H



TRAP

Togni and Spindler[2] have reported a class of non-C$_2$-symmetrical ferrocene-based bisphosphines: the Josiphos-type ligands. Josiphos ligands are in widespread commercial use, having been found effective for Rh-catalyzed hydrogenation of α-acetamidocinnamate, dimethyl itaconate, and β-ketoesters. Because the two phosphine groups are introduced into the ligand in consecutive steps with high yields, a variety of ligands are available with widely differing steric and electronic properties. The ligands have already been applied in three production processes[3], several pilot processes and many other syntheses. For example, PPF-tBu2, a Josiphos type ligand with a di-(tert-butyl)phosphino group, has been applied as the ligand in asymmetric hydrogenation for commercial synthesis of (+)-biotin.[4] Another notable example is the application

of XyliPhos in the Ir-catalyzed hydrogenation of imines for the synthesis of the herbicide (S)-metolachlor[5].

Bophoz[6] is a combination of a phosphine and an aminophosphine and is prepared in 3 steps from ppfa with high overall yields. The ligand is air stable and effective for the hydrogenation of enamides, itaconates and α-keto acid derivatives. As observed for several ligands forming seven-membered chelates, high activities can be reached and TONs up to 10,000 have been claimed. The full scope of this modular ligand class has not yet been explored.

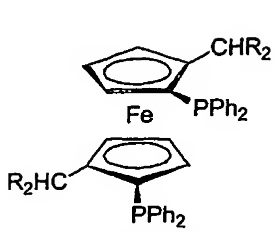
A class of non-C_2-symmetrical, ferrocene-based 1,5-diphosphine ligands, Taniaphos, has been developed by Knochel[7,8]. Compared to the Josiphos ligands, Taniaphos has an additional phenyl ring inserted at the side chain of the Ugi amine. Taniaphos gave excellent results in Rh- and Ru-catalyzed asymmetric hydrogenation. The configuration of α-position of Taniaphos plays an important role in the enantioselectivities and activities. The Taniaphos 1b with αS configuration leads to higher enantioselectivities and activities than 1a with αR configuration in a wide range of asymmetric transformations.

Weissensteiner and Spindler[9] have reported a series of structurally different ferrocene-based 1,5-diphosphine ligands, Walphos. Like Josiphos, Walphos is modular and is also made from the Ugi amine. It shows promise for the enantioselective hydrogenation of olefins and ketones.

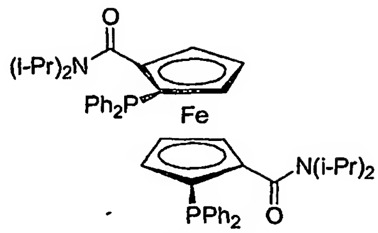
Mandyphos is a bidentate version of ppfa with C_2 symmetry, where in addition to the PPh_2 moieties, R and R' can be used for fine tuning the functionality of the ligand[10]. The scope of this ligand family has not yet been fully explored, but preliminary results indicate high enantioselectivities for the Rh-catalyzed hydrogenation of enamides, itaconates and enol acetates.

The TRAP ligands developed by Ito[11] form 9-membered metallocycles. However, it is not clear whether the cis-isomer, present in small amounts, or the major trans-isomer is responsible for the catalytic activity. Up to now only a few different PR2 fragments have been tested, but it is clear that the choice of R strongly affects the catalytic performance. The Rh complexes work best at very low pressures of 0.5 ± 1 bar and effectively reduces indole-derivatives, enamides and itaconic acid derivatives.

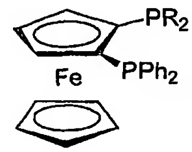
Another class of known ligands exhibit only planar chirality:



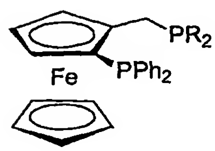
ferroPHOS



JAFAPhos



2



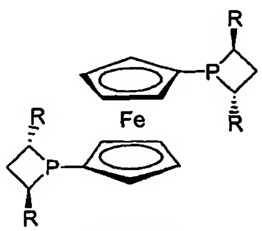
3

Kang[12] reported the C_2-symmetry FerroPHOS with only planar chirality. FerroPHOS ligands are air-stable and are very efficient for the asymmetric hydrogenation of various dehydroamino acid derivitives (up to 99% ee).

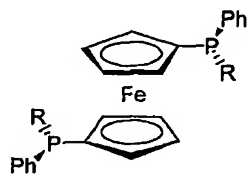
Another C_2-symmetry planar chiral diphosphine, JAFAPhos, has been developed by Jendralla[13]. JAFAPhos gave excellent results in asymmetric hydrogenation, allylic alkylation, Grignard cross coupling and aldol reactions.

Kagan[14] reported plane chiral ferrocene-based bisphosphorus ligands 2 and 3, and up to 95% ee's have been obtained in asymmetric hydrogenation of dimethyl itaconate using these ligands as catalyst.

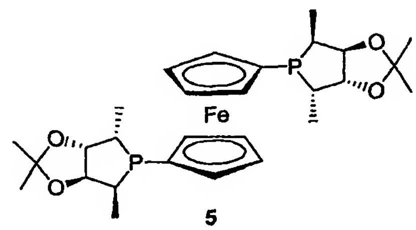
Another class of known diphosphine ligands exhibit chirality only at the phosphorus atoms:



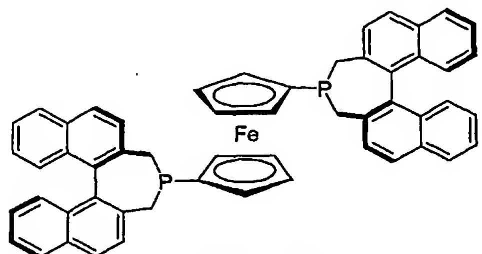
FerroTane



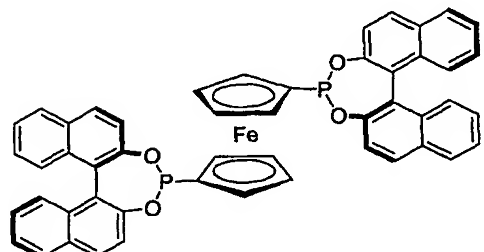
4a: R = o-anisyl
4b: R = 1-naphthyl



5



f-binaphane



6

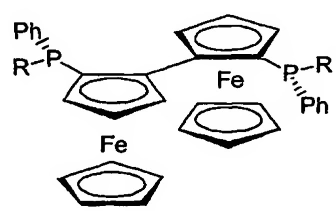
The synthesis of chiral 1,1'-bis(phosphetano) ferrocenes (FerroTANE) has been independently reported by Marinetti[15] and Burk[16]. FerroTANE has been successfully applied in Rh-catalyzed hydrogenation of itaconates and (E)-β-(acylamino) acrylates[17].

Mezzetti[18] and van Leeuwen[19] have independently reported P-chiral ferrocenyl bisphosphines 4a and 4b. These two ligands have shown excellent enantioselectivities (up to 99% ee) for asymmetric hydrogenation of α-dehydroamino acid derivatives.

Zhang has reported a 1,1'-bis(Phospholanyl) ferrocene ligand 5 with ketal substitutes at the 3 and 4 positions. [20] The ligand has shown excellent enantioselectivities in hydrogenation of β-dehydroamino acid derivatives. The ketal groups of the ligand are important for achieving the high enantioselectivity, since the corresponding ligand without ketal groups only provides moderate ee's. Zhang has also developed a 1,1'-bis(dinaphthophosphepinyl) ferrocene ligand, f-binaphane, which has been successfully applied in the Ir-catalyzed hydrogenation of acyclic aryl imines. [21]

Reetz has developed a binaphthol-derived ferrocene-based bisphosphonite ligand 6[22], which has shown excellent reactivities and enantioselectivities in Rh-catalyzed hydrogenation of itaconates and α-dehydroamino acid derivatives.

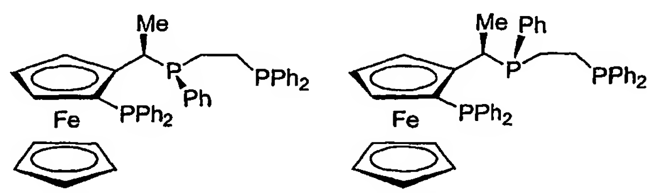
Another class of known ligands exhibits both planar and phosphorus chirality:



7a: R = 1-naphthyl
7b: R = 2-biphenylyl

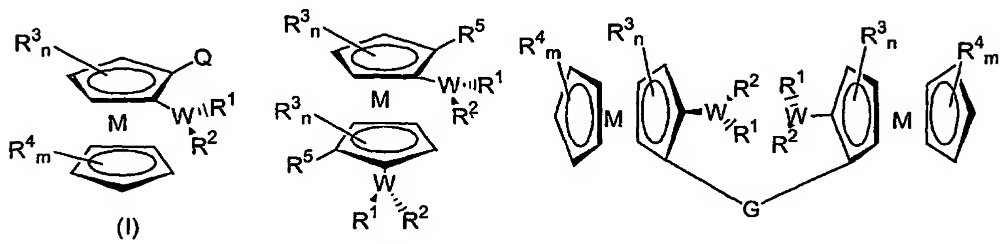
Van Leeuwen has reported ferrocene-based bisphosphines combining planar and phosphorus chirality 7a and 7b[23]. These two ligands have shown excellent enantioselectivities (up to 99% ee) for asymmetric allylic alkylations.

Thus, most of the known ferrocene-based diphosphines contain planar and carbon chirality, only planar chirality or only phosphorus chirality. More recently, Togni reported the first tridentate ferrocene-based phosphine ligand 12 combining planar, phosphorus and carbon chirality. [24]



$(R)_c$-$(S)_{Fe}$-$(S)_P$-12 $(R)_c$-$(S)_{Fe}$-$(R)_P$-12

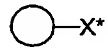
In our co-pending application GB0400720.9 we describe ligands having Formula (I), (II) or (III):



(I) (II) (III)

wherein $R^{1\text{-}5}$, W, Q, n, m and G are variously defined, and a process for making such ligands. However, the process described therein is found to be more generally applicable to the production of various chiral ligands.

According to the present invention there is provided a process for the production of chiral ligands comprising providing a starting material of Formula (A):



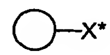
(A)

wherein X* is a chiral or achiral directing group; and

 is an optionally substituted mono- or polycyclic aryl or cycloalkyl group; ortholithiating the substrate; converting the ortho-lithiated substrate to a phosphine group having the formula $-PR^1 R^{1''}$, R^1 and $R^{1''}$ being different from each other and independently selected from substituted and unsubstituted, branched- and straight-chain alkyl, alkoxy, alkylamino, substituted and unsubstituted cycloalkyl, substituted and unsubstituted cycloalkoxy, substituted and unsubstituted cycloalkylamino, substituted and unsubstituted carbocyclic aryl, substituted and unsubstituted carbocyclic aryloxy, substituted and unsubstituted heteroaryl, substituted and unsubstituted heteroaryloxy, substituted and unsubstituted carbocyclic arylamino and substituted and unsubstituted heteroarylamino, wherein the or each heteroatom is independently selected from sulphur, nitrogen, and oxygen;
and optionally or if necessary converting X* to a different grouping to produce a chiral ligand.

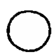
 is, in one such process according to the invention, one aromatic ring (optionally further substituted) of a metallocene compound.

Also provided in accordance with the invention is a process for the production of chiral ligands comprising providing a starting material of Formula (A):

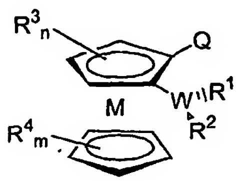


(A)

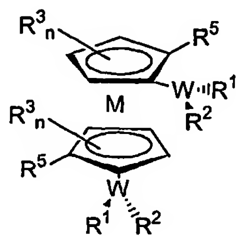
wherein X* is a chiral or achiral directing group; and

 is an optionally substituted mono- or polycyclic aryl or cycloalkyl group; ortholithiating the substrate; reacting the ortholithiated substrate with an R^1 substituted phosphine or arsine, R^1 being selected from substituted and unsubstituted, branched- and straight-chain alkyl, substituted and unsubstituted cycloalkyl, substituted and unsubstituted carbocyclic aryl, and substituted and unsubstituted heteroaryl wherein the or each heteroatom is independently selected from sulphur, nitrogen, and oxygen; and then with an $R^{1''}$-bearing Grignard reagent or organolithium compound, $R^{1''}$ being different from R^1 and being selected from substituted and unsubstituted, branched- and straight-chain alkyl, substituted and unsubstituted cycloalkyl, substituted and unsubstituted carbocyclic aryl, and substituted and unsubstituted heteroaryl wherein the or each heteroatom is independently selected from sulphur, nitrogen, and oxygen; and optionally or if necessary converting X* to a different grouping to produce a chiral ligand;

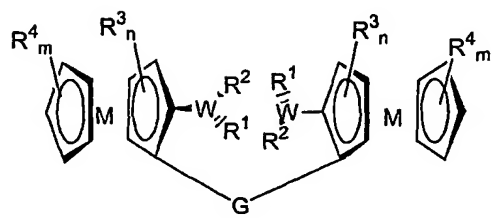
with the exception that the chiral ligand is <u>not</u> a ligand having Formula (I), (II) or (III):



(I)



(II)



(III)

wherein $R^{1\text{-}5}$, W, Q, n, m and G are as defined in GB0400720.9.

 is, in one such process according to the invention, one aromatic ring (optionally further substituted) of a metallocene compound.

The process of the invention may be used in the production of phosphine or arsine ligands having up to three elements of chirality; planar chirality, chirality at phosphorus (or arsenic), and optionally chirality at carbon.

In the following description reference will be made for convenience to processes for the production of phosphine ligands. It should be understood that although processes for producing phosphine ligands are the preferred processes in accordance with the invention, the corresponding processes for producing arsine ligands are also within the scope of the invention.

Similarly, when the chiral ligand obtained by the process of the invention is a metallocene ligand, processes for producing ferrocene based ligands are preferred, but other suitable metals may be used in the metallocene ligands obtained by the process of the invention, and hence reference is made herein to metallocenes generally.

The invention further provides chiral ligands obtained by the process of the invention. Examples of such ligands include metallocene-based phosphine ligands having planar, phosphorus and carbon chirality.

The invention further provides chiral ligands (other than those of Formula (I), (II) or (III)) obtained by the process of the invention. Examples of such ligands include metallocene-based phosphine ligands having planar, phosphorus and carbon chirality.

Ligands obtained by a process according to the invention have particular advantages over prior art ligands because the provision of up to three chiralities allows the designer of a ligand greater scope than has hitherto been the case to design ligands for a particular purpose.

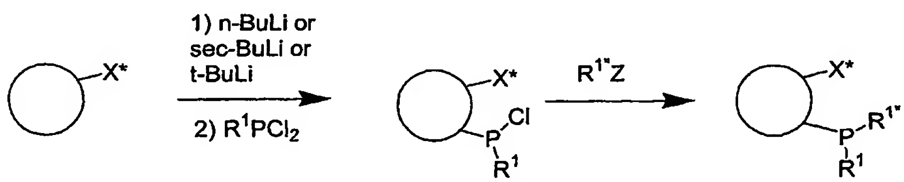
The introduction of phosphorus chirality may enhance the chiral discrimination produced by the catalyst when a matching among the planar chirality, carbon

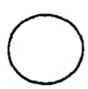
chirality and the chirality of phosphorus can be achieved. A matching catalyst may give high ee and a mismatching one may give low ee.

Also provided in accordance with the invention is a transition metal complex containing transition metal coordinated to the ligand produced by the process of the invention. The metal is preferably a Group VIb or a Group VIII metal.

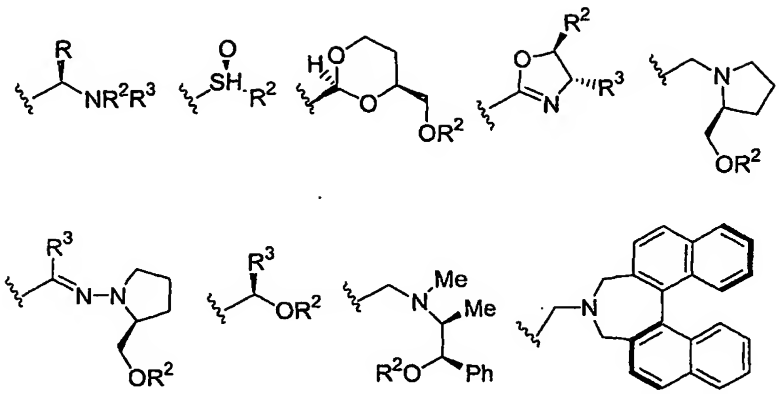
Preferably X* is an ortho directing group.

Synthesis of phosphorus chiral phosphines may be effected in accordance with the invention with the use of a suitable chiral *ortho*-directing group, for example in accordance with the following scheme:



Wherein  is an optionally substituted mono- or polycyclic aryl or cycloalkyl group and wherein $R^{1"}Z$ is an organoalkali species or Grignard reagent

Examples of suitable chiral directing groups:

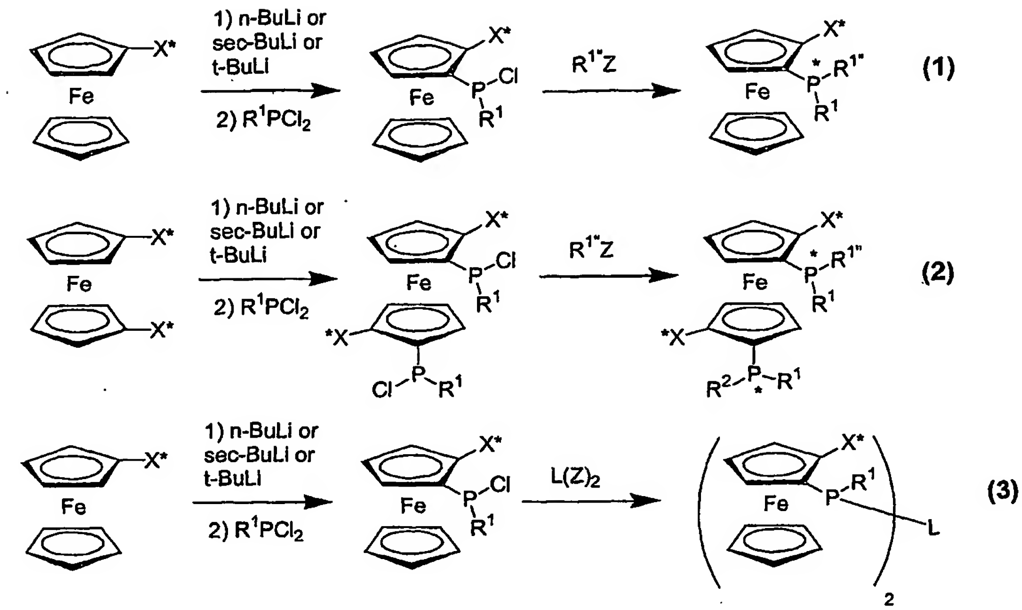


Wherein R, R^2 and R^3 are independently selected from substituted and unsubstituted, branched- and straight-chain alkyl, substituted and unsubstituted cycloalkyl, substituted and unsubstituted carbocyclic aryl, and substituted and unsubstituted heteroaryl wherein the or each heteroatom is independently selected from sulphur, nitrogen, and oxygen.

 is, in one such process according to the invention, one aromatic ring (optionally further substituted) of a metallocene compound.

And wherein

For example, synthesis of ferrocene-based phosphorus chiral phosphines may be effected with the use of a suitable chiral *ortho*-directing group, for example in accordance with the following schemes:



Examples of suitable chiral directing groups are as previously specified.

wherein, in relation to scheme 3, L is a linker. For example, L may be selected from ferrocene, diphenyl ethers, xanthenes, 2,3-benzothiophene, 1,2-benzene, succinimides and many others. Conveniently, such dianionic linkers may be made from a corresponding di-halo precursor, eg:

Certain suitable dianionic linkers may be represented as follows:

However, ferrocene is a preferred linker in accordance with the invention.

(Similar schemes may be used to synthesise the corresponding arsines, and other metallocenes, and may be applicable to other ring systems. Also, for

convenience, these schemes are depicted with ferrocene-based substrates, but they may be also be applicable to other aromatic-based substrates.)

Accordingly, the invention provides a method for preparing a phosphine ligand chiral at phosphorus comprising providing an optionally substituted mono- or polyaromatic or cycloalkyl substrate having a chiral or achiral directing substituent on at least one ring, and subjecting the substrate to an ortho-lithiation step before subsequently converting the ortho-lithiated substrate to a phosphine group having the formula $-PR^1R^{1''}$ or PR^1L, wherein L is a linker as previously defined and wherein, $R^1$and $R^{1''}$ are different from each other and are independently selected from substituted and unsubstituted, branched- and straight-chain alkyl, substituted and unsubstituted cycloalkyl, substituted and unsubstituted carbocyclic aryl, and substituted and unsubstituted heteroaryl wherein the or each heteroatom is independently selected from sulphur, nitrogen, and oxygen, and optionally or if necessary converting the directing substituent to a chiral group, or to a different chiral group.

Accordingly, the invention provides a method for preparing a phosphine ligand chiral at phosphorus comprising providing a metallocene-based substrate having a chiral or achiral directing substituent on at least one ring, and subjecting the substituted metallocene to an ortho-lithiation step before subsequently converting the ortho-lithiated substrate to a phosphine group having the formula $-PR^1R^{1''}$ or PR^1L, wherein L is a linker as previously defined

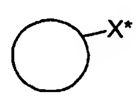
and wherein, $R^1$and $R^{1''}$ are different from each other and are independently selected from substituted and unsubstituted, branched- and straight-chain alkyl, substituted and unsubstituted cycloalkyl, substituted and unsubstituted carbocyclic aryl, and substituted and unsubstituted heteroaryl wherein the or each heteroatom is independently selected from sulphur, nitrogen, and oxygen, and optionally or if necessary converting the directing substituent to a chiral group, or to a different chiral group.

The invention also provides a method for preparing an arsine ligand chiral at arsenic comprising providing an optionally substituted mono- or polyaromatic or cycloalkyl substrate having a chiral or achiral directing substituent on at least one ring, and subjecting the substrate to an ortho-lithiation step before subsequently converting the ortho-lithiated substrate to an arsine group having the formula $-AsR^1R^{1''}$ or AsR^1L, wherein L is a linker as previously defined and wherein, $R^1$and $R^{1''}$ are different from each other and are independently selected from substituted and unsubstituted, branched- and straight-chain alkyl, substituted and unsubstituted cycloalkyl, substituted and unsubstituted carbocyclic aryl, and substituted and unsubstituted heteroaryl wherein the or each heteroatom is independently selected from sulphur, nitrogen, and oxygen, and optionally or if necessary converting the directing substituent to a chiral group, or to a different chiral group.

The invention also provides a method for preparing an arsine ligand chiral at arsenic comprising providing a metallocene-based substrate having a chiral or achiral directing substituent on at least one ring, and subjecting the substituted metallocene to an ortho-lithiation step before subsequently converting the ortho-lithiated substrate to an arsine group having the formula $-AsR^1R^{1''}$ or AsR^1L, wherein L is a linker as previously defined and wherein, $R^1$and $R^{1''}$ are independently selected from substituted and unsubstituted, branched- and straight-chain alkyl, substituted and unsubstituted cycloalkyl, substituted and unsubstituted carbocyclic aryl, and substituted and unsubstituted heteroaryl wherein the or each heteroatom is independently selected from sulphur, nitrogen, and oxygen, and optionally or if necessary converting the directing substituent to a chiral group, or to a different chiral group.

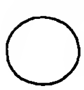
Methods in accordance with the invention for the preparation of chiral ligands will now be more particularly described.

For example, one such method comprises providing a substrate of the Formula (A):



(A)

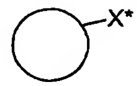
wherein

 is an optionally substituted mono- or polycyclic aryl or cycloalkyl group;

X* is chiral directing group, and is preferably selected from the group as previously defined; ortholithiating the substrate; reacting the ortholithiated substrate with an R^1 substituted halophosphine or haloarsine, R^1 being selected from substituted and unsubstituted, branched- and straight-chain alkyl, substituted and unsubstituted cycloalkyl, substituted and unsubstituted carbocyclic aryl, and substituted and unsubstituted heteroaryl wherein the or each heteroatom is independently selected from sulphur, nitrogen, and oxygen; and then with an $R^{1''}$-bearing Grignard reagent or organoalkali (preferably organolithium) compound, $R^{1''}$ being different from R^1 and being selected from substituted and unsubstituted, branched- and straight-chain alkyl, substituted and unsubstituted cycloalkyl, substituted and unsubstituted carbocyclic aryl, and substituted and unsubstituted heteroaryl wherein the or each heteroatom is independently selected from sulphur, nitrogen, and oxygen;
and optionally converting X* to a different grouping to produce a chiral ligand.

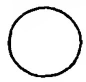
 is, in one such process according to the invention, one aromatic ring (optionally further substituted) of a metallocene compound.

Another method comprises providing a compound of the Formula (A):



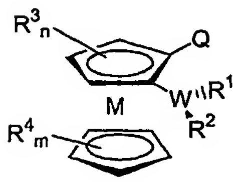
(A)

wherein

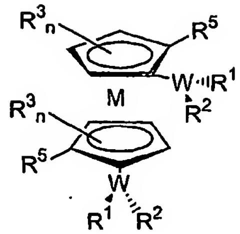
 is an optionally substituted mono- or polycyclic aryl or cycloalkyl group;

X* is chiral directing group, and is preferably selected from the group as previously defined; ortholithiating the substrate; reacting the ortholithiated substrate with an R^1 substituted halophosphine or haloarsine, R^1 being selected from substituted and unsubstituted, branched- and straight-chain alkyl, substituted and unsubstituted cycloalkyl, substituted and unsubstituted carbocyclic aryl, and substituted and unsubstituted heteroaryl wherein the or each heteroatom is independently selected from sulphur, nitrogen, and oxygen; and then with an $R^{1''}$-bearing Grignard reagent or organoalkali (preferably organolithium) compound, $R^{1''}$ being selected from substituted and unsubstituted, branched- and straight-chain alkyl, substituted and unsubstituted cycloalkyl, substituted and unsubstituted carbocyclic aryl, and substituted and unsubstituted heteroaryl wherein the or each heteroatom is independently selected from sulphur, nitrogen, and oxygen;

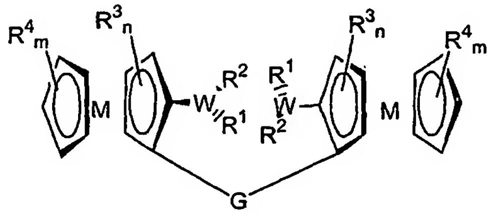
and optionally converting X* to a different grouping to produce a chiral ligand; with the exception that the chiral ligand is <u>not</u> a ligand having Formula (I), (II) or (III):



(I)



(II)

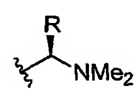


(III)

wherein R^{1-5}, W, Q, n, m and G are as defined in GB0400720.9.

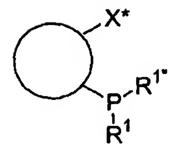
 is, in one such process according to the invention, one aromatic ring (optionally further substituted) of a metallocene compound.

One particularly preferred X* group in each of the above methods is



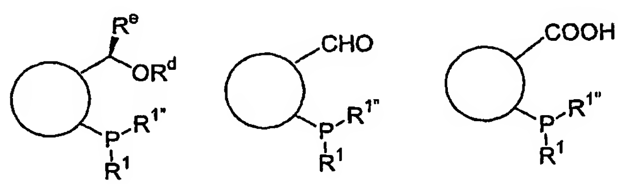
The ortho-lithiation step is preferably a mono-ortho-lithiation step using n-butyllithium, sec-butyllithium or tert-butyllithium. The resulting monolithium compound is preferably reacted *in situ* with a dichlorophosphine of the formula R^1PCl_2 followed by reacting with an organometallic reagent of the formula $R^{1''}Z$, wherein R^1 and $R^{1''}$ are as defined above; Z is Li or MgY wherein Y is a halide.

These steps may be performed to obtain a phosphorus chiral compound having formula (C) (wherein the aromatic or cycloaliphatic ring(s) is/are optionally substituted:



(C)

The synthesis preferably proceeds by converting compound (C) to compound D, E, or F:



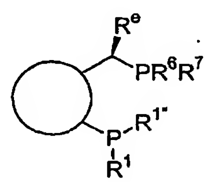
(D) (E) (F)

wherein R^d is an acyl group, R^e is selected from hydrogen, substituted and unsubstituted, branched- and straight-chain alkyl, substituted and unsubstituted cycloalkyl, substituted and unsubstituted carbocyclic aryl, and substituted and unsubstituted heteroaryl wherein the or each heteroatom is independently selected from sulphur, nitrogen, and oxygen, and R^1, $R^{1"}$ are as previously defined;

and then:

reacting compound D with a secondary phosphine of the formula R^6R^7PH wherein R^6 and R^7 are the same or different, and are independently selected from substituted and unsubstituted, branched- and straight-chain alkyl, alkoxy, alkylamino, substituted and unsubstituted cycloalkyl, substituted and unsubstituted cycloalkoxy, substituted and unsubstituted cycloalkylamino, substituted and unsubstituted carbocyclic aryl, substituted and unsubstituted

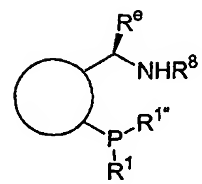
carbocyclic aryloxy, substituted and unsubstituted heteroaryl, substituted and unsubstituted heteroaryloxy, substituted and unsubstituted carbocyclic arylamino and substituted and unsubstituted heteroarylamino, wherein the or each heteroatom is independently selected from sulphur, nitrogen, and oxygen; and R^8 is selected from hydrogen, substituted and unsubstituted, branched- and straight-chain alkyl, substituted and unsubstituted cycloalkyl, substituted and unsubstituted carbocyclic aryl, and substituted and unsubstituted heteroaryl wherein the or each heteroatom is independently selected from sulphur, nitrogen, and oxygen to obtain the diphosphine combining planar, phosphorus and carbon chirality having formula G:



(G)

or;

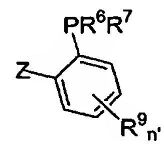
reacting compound D with an amine of the formula R^8NH_2 wherein R^8 is selected from hydrogen, substituted and unsubstituted, branched- and straight-chain alkyl, substituted and unsubstituted cycloalkyl, substituted and unsubstituted carbocyclic aryl, and substituted and unsubstituted heteroaryl wherein the or each heteroatom is independently selected from sulphur, nitrogen, and oxygen, to obtain compound H:



(H)

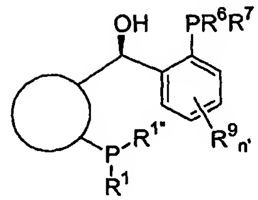
or;

reacting compound D with an amine of the formula J:



(J)

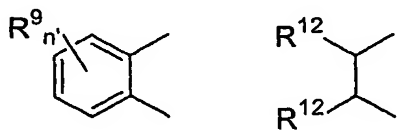
wherein R^6 and R^7 are as previously defined, R^9 is selected from hydrogen, halogen, OR^{10}, SR^{10}, $NR^{10}R^{11}$, substituted and unsubstituted, branched- and straight-chain alkyl, substituted and unsubstituted cycloalkyl, substituted and unsubstituted carbocyclic aryl, and substituted and unsubstituted heteroaryl wherein the or each heteroatom is independently selected from sulphur, nitrogen, and oxygen; wherein R^{10}, R^{11} are the same or different and are independently selected from hydrogen, substituted and unsubstituted, branched- and straight-chain alkyl, substituted and unsubstituted cycloalkyl, substituted and unsubstituted carbocyclic aryl, and substituted and unsubstituted heteroaryl wherein the or each heteroatom is independently selected from sulphur, nitrogen, and oxygen, n' is 0 to 4, and Z is MgY (Y being a halide) or Li, to obtain compound K:



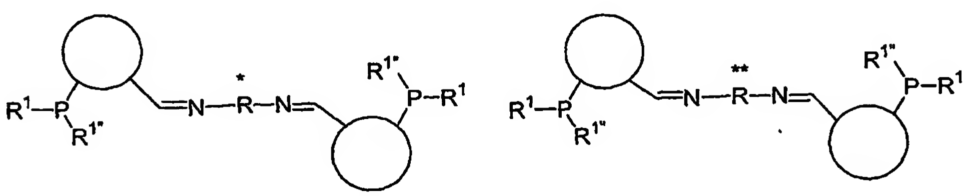
(K)

or;

reacting compound D with an amine of the formula $H_2N\text{-}R^*\text{-}NH_2$ or $H_2N\text{-}R^{**}\text{-}NH_2$ wherein R* and R** are selected from the group consisting of:



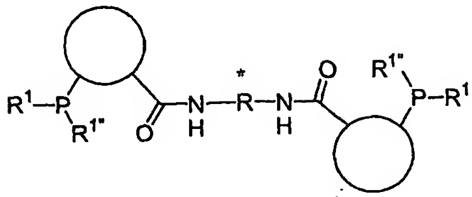
wherein R^9 is as previously defined; R^{12} is selected from hydrogen, substituted and unsubstituted, branched- and straight-chain alkyl, substituted and unsubstituted cycloalkyl, substituted and unsubstituted carbocyclic aryl, and substituted and unsubstituted heteroaryl wherein the or each heteroatom is independently selected from sulphur, nitrogen, and oxygen; or $(R^{12})_2$ is $-(CH_2)_{m'}-$, n' is 0 to 4; and m' is 1 to 8, to obtain compounds L and M:



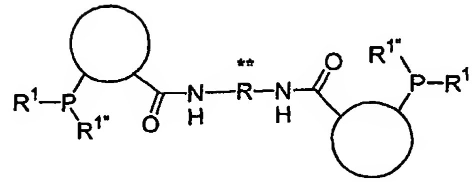
(L) (M)

or;

reacting compound E with an amine of the formula $H_2N\text{-}R^*\text{-}NH_2$ or $H_2N\text{-}R^{**}\text{-}NH_2$ wherein R* and R** are, as previously defined, to obtain compounds O and P:

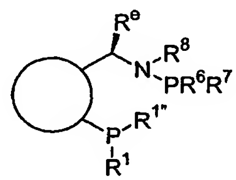


(O)



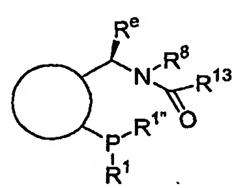
(P)

Compound H may be reacted with a halophosphine of the formula R^6R^7PY wherein R^6, R^7 are, as previously defined, and Y is chlorine, bromine or iodine, to obtain compound Q:



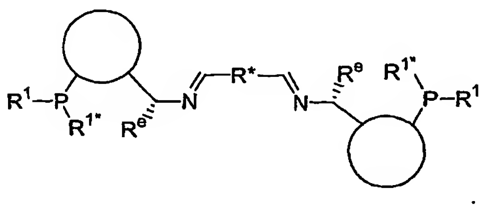
(Q)

Alternatively, compound H may be reacted with an acid derivative of the formula $R^{13}COY$ wherein R^{13} is selected from hydrogen, substituted and unsubstituted, branched- and straight-chain alkyl, substituted and unsubstituted cycloalkyl, substituted and unsubstituted carbocyclic aryl, and substituted and unsubstituted heteroaryl wherein the or each heteroatom is independently selected from sulphur, nitrogen, and oxygen, and Y is a halide, a sulphate, an imidazole, $R^{13}COO$- or hydrogen, to obtain compound R:

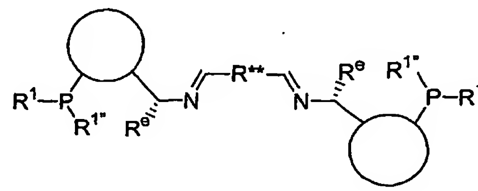


(R)

Alternatively compound H (in which R^8 is hydrogen) may be reacted with an aldehyde of the formula OHC-R*-CHO or OHC-R**-CHO wherein R* and R are as previously defined to obtain the compounds having Formulae S and T:

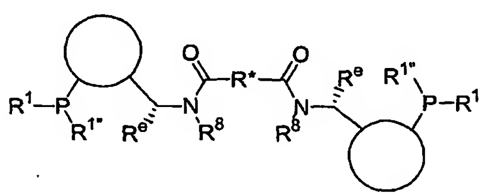


(S)

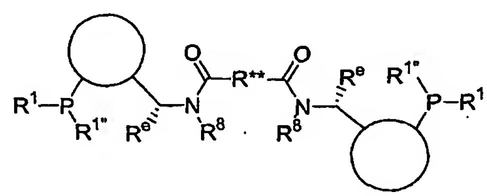


(T)

Alternatively compound H may be reacted with an acid derivative of the formula YOC-R*-COY and YOC-R**-COY wherein R*, R** and Y are, as previously defined, to obtain the compounds having Formulae U and V:

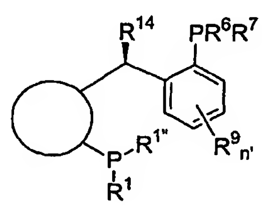


(U)



(V)

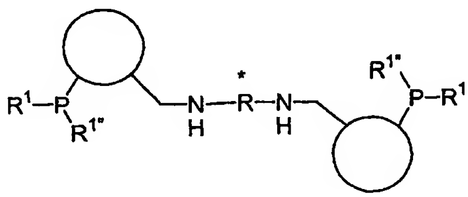
Compound K may be converted into compound X:



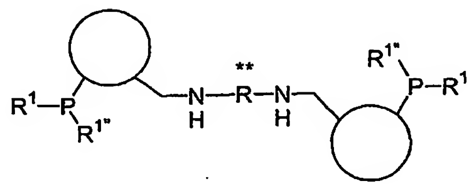
(K)

wherein R^{14} is selected from OR^{10}, SR^{10}, NHR^{10} and $NR^{10}R^{11}$, wherein R^{10}, R^{11} are as previously defined.

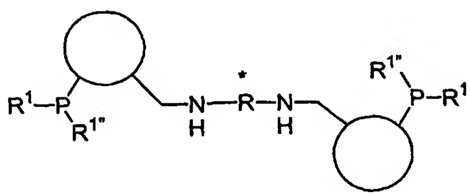
Compounds L, M, O, P, S, T, U, V may be reduced to obtain respective compounds L*, M*, O*, P*, S*, T*, U*,V*:



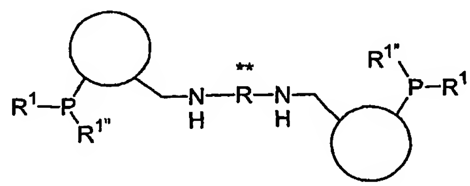
(L*)



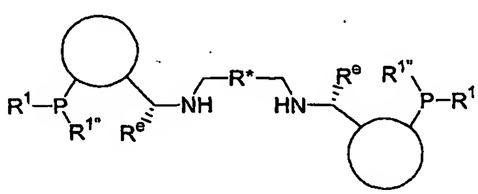
(M*)



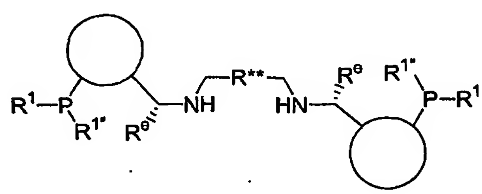
(O*)



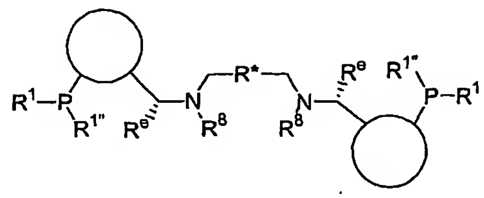
(P*)



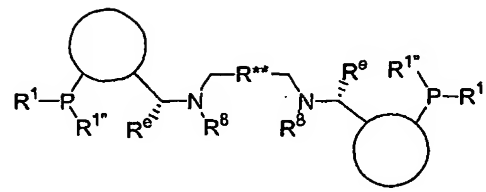
(S*)



(T*)

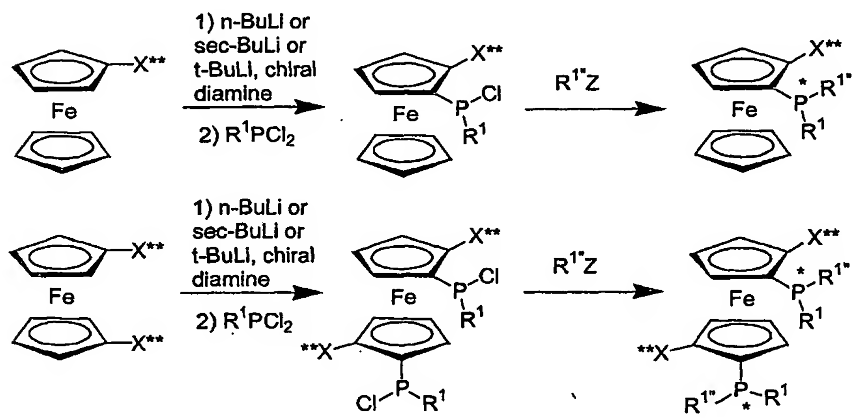


(U*)

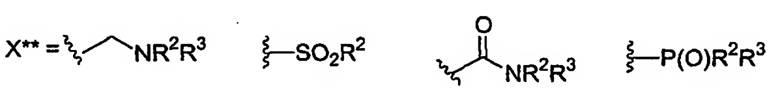


(V*)

Synthesis of metallocene-based phosphines chiral at phosphorus may be also effected with the use of enantioselective ortho-lithiation (ferrocene-based substrates are indicated below and are illustrative of aromatic and cycloaliphatic substrates generally in connection with the process of the invention):

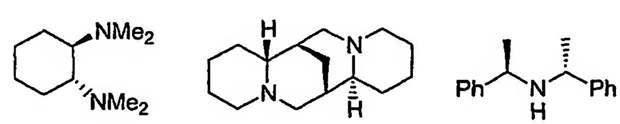


Examples of suitable achiral directing groups:



(wherein R^2 and R^3 are as previously defined)

Suitable Chiral diamines include:



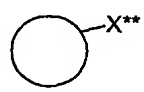
Accordingly, the invention provides a method for preparing a chiral diphosphine ligand comprising a metallocene-based substrate having an achiral directing

substituent on one or both rings, and subjecting the substituted metallocene to an enantioselective ortho-lithiation step before subsequently converting the ortho-lithiated substrate to a phosphorus chiral phosphine.

Whilst the use of an auxiliary chiral compound (such as the chiral diamine) in the ortholithiation step may be preferred in some circumstances, where direct synthesis of a chiral product (in enantiomeric excess) is desired, it is also possible to ortholithiate in the absence of such a chiral auxiliary, and then resolve the enantiomeric product mixture at the end of the synthesis.

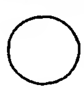
(This method is also applicable to arsines.)

Thus, one method according to the present invention for preparing chiral ligands comprises providing a substrate of the formula A*:



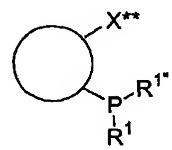
(A*)

wherein

 is an optionally substituted mono- or polycyclic aryl or cycloalkyl group;

wherein X** is an achiral directing group, and is preferably as previously defined; and subjecting the compound to enantioselective mono-ortho-lithiation using n-butyllithium or sec-butyllithium or tert- butyllithium in the presence of a homochiral tertiary amine, and reacting the resulting chiral monolithium

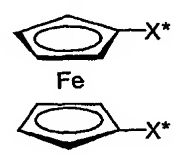
compound *in situ* with a dichlorophosphine of the formula R^1PCl_2 followed by reacting with an organometallic reagent of the formula $R^{1''}M$, wherein R^1 and $R^{1''}$ are as defined hereinabove; M is Li or MgX wherein X is a halide, to obtain phosphorus chiral compound having formula C*:



(C*)

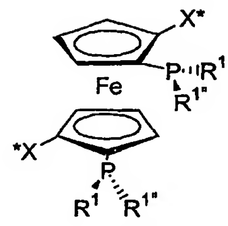
and optionally or if necessary further converting compound C* to the desired chiral ligand.

One method according to the invention for preparing a ferrocene-based chiral ligand comprises providing a compound of the Formula B*:



(B*)

wherein X* is as previously defined; and subjecting the compound to bis-ortho-lithiation using n-butyllithium, sec-butyllithium or tert- butyllithium, and reacting the resulting bislithium compound *in situ* with a dichlorophosphine of the formula R^1PCl_2 followed by reacting with an organometallic reagent of the formula $R^{1''}Z$, wherein R^1 and $R^{1''}$ are as previously defined; Z is Li or MgY wherein Y is a halide, to obtain a phosphorus chiral compound having formula B***:



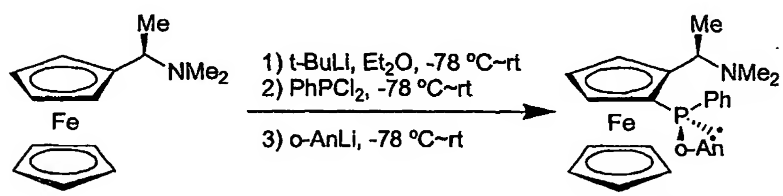
(B***)

and optionally or if necessary converting compound B*** to the desired chiral ligand.

The invention will now be more particularly illustrated with reference to the following Examples.

Example 1

(R_c, S_{Fe}, S_P)-2-[(1-N,N-Dimethylamino)ethyl]-1-[(2-methoxyphenyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-2]:



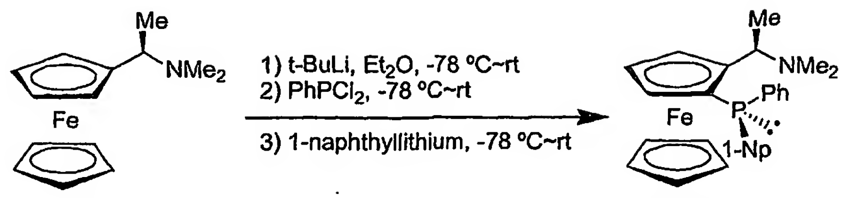
(R)-1 **R_C-S_{Fe}-S_P-2**

To a solution of (R)-N,N-dimethyl-1-ferrocenylethylamine [(R)-Ugi's amine, (R)-**1**] (3.86 g, 15 mmol) in Et_2O (50 mL) was added 1.7 M t-BuLi solution in pentane (9.7 mL, 16.5 mmol) over 10 min via a syringe at –78 °C. After addition

was completed, the mixture was warmed to room temperature, and stirred for 1.5 h at room temperature. The resulting red solution was cooled to –78 °C again, and dichlorophenylphosphine (2.24 mL, 16.5 mmol) was added in one portion. After stirring for 10 min at –78 °C, the mixture was slowly warmed to room temperature, and stirred for 1.5 h at room temperature. The mixture was then cooled to –78 °C again, and a solution of (2-methoxy)phenyllithium [prepared from 2-bromoanisole (3.32 g, 17.7 mmol) and 1.7 M t-BuLi solution in pentane (20.8 mL, 35.4 mmol) in Et_2O (90 mL) at –78 °C] was added slowly via a cannula. The mixture was warmed to room temperature overnight, and filtered through a pad of Celite. The filtrate was concentrated, and the residue was purified by chromatography (SiO_2, hexane-EtOAc-Et_3N = 85:10:5) to afford the title compound (6.50 g, 92%) as orange crystals. ^1H NMR ($CDCl_3$, 400.13 MHz): δ 1.29 (d, 3H, J = 6.5 Hz); 1.80 (s, 6H); 3.91 (s, 3H); 3.97 (s, 6H, overlap); 4.11 (m, 1H), 4.25 (t, 1H, J = 2.2 Hz); 4.37 (br. s, 1H); 6.87 (m, 1H); 6.94 (dd, 1H, J = 8.3 and 6.7 Hz); 7.12 ~ 7.23 (m, 6H); 7.31 (m, 1H); ^{31}P NMR ($CDCl_3$, 162 MHz): δ –38.82. The absolute configuration of (R_c, S_{Fe}, S_P)-**2** was determined by single-crystal X-ray diffraction analysis.

Example 2

(R_c, S_{Fe}, S_P)-2-[(1-N,N-Dimethylamino)ethyl]-1-[(1-naphthyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-3]:



(R)-1

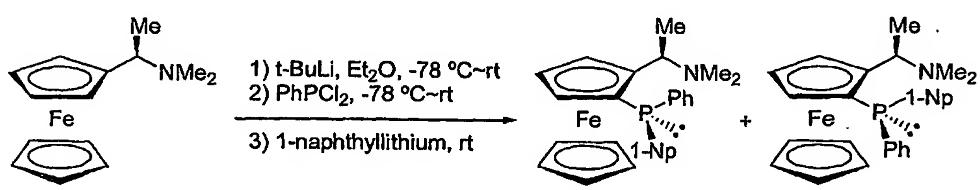
(R_C-S_{Fe}-S_P)-3

To a solution of (R)-N,N-dimethyl-1-ferrocenylethylamine [(R)-Ugi's amine, (R)-1] (5.15 g, 20 mmol) in Et_2O (60 mL) was added 1.7 M t-BuLi solution in pentane (12.94 mL, 22 mmol) over 10 min via a syringe at –78 °C. After addition was completed, the mixture was warmed to room temperature, and stirred for 1.5 h at room temperature. The resulting red solution was cooled to –78 °C again, and dichlorophenylphosphine (2.99 mL, 22 mmol) was added in one portion. After stirring for 10 min at –78 °C, the mixture was slowly warmed to room temperature, and stirred for 1.5 h at room temperature. The mixture was then cooled to –78 °C again, and a solution of 1-naphthyllithium [prepared from 1-bromonaphthalene (5.38 g, 26 mmol) and 1.7 M t-BuLi solution in pentane (30.6 mL, 52 mmol) in Et_2O (120 mL) at –78 °C] was added slowly via a cannula. The mixture was warmed to room temperature overnight, and filtered through a pad of Celite. The filtrate was concentrated, and the residue was purified by chromatography (SiO_2, hexane-EtOAc-Et_3N = 90:6:4) to afford the title compound (8.75 g, 89%) as orange crystals. ^1H NMR ($CDCl_3$, 400.13 MHz): δ 1.33 (d, 3H, J = 6.8 Hz); 1.91 (s, 6H); 3.59 (s, 5H); 4.00 (m, 1H); 4.17 (m, 1H); 4.26 (t, 1H, J = 2.2 Hz); 4.38 (m, 1H); 7.13 ~ 7.2 (m, 5H); 7.39 (t, 1H, J = 6.7

Hz); 7.43 ~7.54 (m, 2H); 7.60 ~7.63 (m, 1H); 7.87 (dd, 2H, J = 9.7 and 9.2 Hz), 9.33 (dd, 1H, J = 7.6 and 7.0 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ –38.73.

Example 3

(R_c, S_{Fe}, S_P)-2-[(1-N,N-Dimethylamino)ethyl]-1-[(1-naphthyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-3] and (R_c, S_{Fe}, R_P)-2-[(1-N,N-Dimethylamino)ethyl]-1-[(1-naphthyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, R_P)-4]:



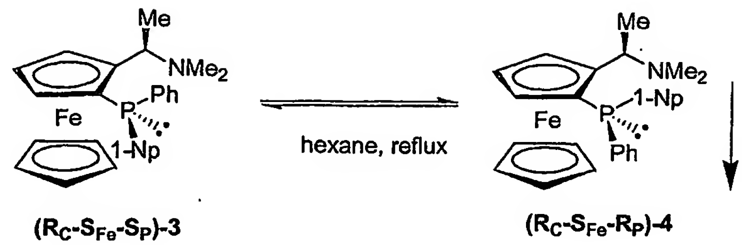
(R)-1 (R_C-S_{Fe}-S_P)-3 (R_C-S_{Fe}-R_P)-4

To a solution of (R)-N,N-dimethyl-1-ferrocenylethylamine [(R)-Ugi's amine, (R)-1] (1.29 g, 5 mmol) in Et_2O (15 mL) was added 1.7 M t-BuLi solution in pentane (3.2 mL, 5.5 mmol) over 10 min via a syringe at –78 °C. After addition was completed, the mixture was warmed to room temperature, and stirred for 1.5 h at room temperature. The resulting red solution was cooled to –78 °C again, and dichlorophenylphosphine (0.75 mL, 5.5 mmol) was added in one portion. After stirring for 10 min at –78 °C, the mixture was slowly warmed to room temperature, and stirred for 1.5 h at room temperature. Then to the mixture a

solution of 1-naphthyllithium [prepared from 1-bromonaphthalene (1.35 g, 6.5 mmol) and 1.7 M t-BuLi solution in pentane (7.6 mL, 13 mmol) in Et_2O (30 mL) at –78 °C] was added via a cannula at room temperature. The mixture was stirred overnight at room temperature and filtered through a pad of Celite. The filtrate was concentrated, and the residue was purified by chromatography (SiO_2, hexane-EtOAc-Et3N = 85:10:5) to afford the title compound (2.21 g, 90%) as a mixture of two isomers. The ratio of (R_c, S_{Fe}, S_P)-**3** to (R_c, S_{Fe}, R_P)-**4** is about 5:1. As (R_c, S_{Fe}, R_P)-**4** is insoluble in cold hexane and (R_c, S_{Fe}, S_P)-**3** is very soluble in cold hexane, the two isomers can be easily separated by crystallization from hexane. (R_c, S_{Fe}, R_P)-**4** : ^{1}H NMR ($CDCl_3$, 400.13 MHz): δ 1.25 (d, 3H, *J* = 6.8 Hz); 1.60 (s, 6H); 3.88 (br. s, 1H); 4.00 (s, 5H); 4.16 (m, 1H), 4.29 (t, 1H, *J* = 2.2 Hz); 4.42 (br. s, , 1H); 7.16 ~ 7.19 (m, 1H); 7.28 ~ 7.29 (m, 5H), 7.32 ~ 7.35 (m, 1H); 7.59 ~ 7.63 (m, 2H); 7.69 (d, *J* = 8.2 Hz); 7.76 (d, *J* = 7.6 Hz); 8.45 (m, 1H). ^{31}P NMR ($CDCl_3$, 162 MHz): δ –31.36. The absolute configuration of (R_c, S_{Fe}, R_P)-**4** was determined by single-crystal X-ray diffraction analysis.

Example 4

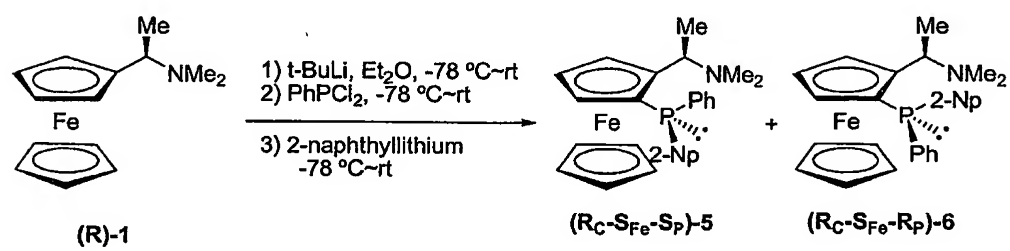
(R_c, S_{Fe}, R_P)-2-[(1-N,N-Dimethylamino)ethyl]-1-[(1-naphthyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, R_P)-4]:



A solution of (R_c, S_{Fe}, S_P)-**3** (491 mg, 1.0 mmol) in hexane (5 mL) was refluxed overnight. After cooling to room temperature, the precipitate was filtered and washed with cold hexane to give the pure (R_c, S_{Fe}, R_P)-**4**.

Example 5

(R_c, S_{Fe}, S_P)-2-[(1-N,N-Dimethylamino)ethyl]-1-[(2-naphthyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-5] and (R_c, S_{Fe}, R_P)-2-[(1-N,N-Dimethylamino)ethyl]-1-[(2-naphthyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, R_P)-6]:

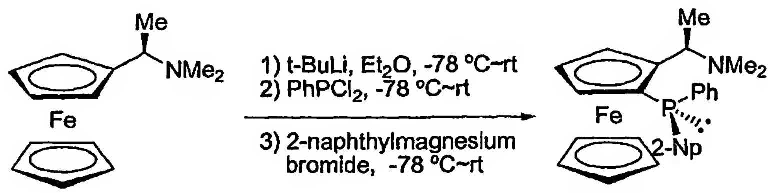


To a solution of (R)-N,N-dimethyl-1-ferrocenylethylamine [(R)-Ugi's amine, (R)-**1**] (2.57 g, 5 mmol) in Et_2O (15 mL) was added 1.7 M t-BuLi solution in pentane (6.4 mL, 11 mmol) over 10 min via a syringe at –78 °C. After addition was

completed, the mixture was warmed to room temperature, and stirred for 1.5 h at room temperature. The resulting red solution was cooled to –78 °C again, and dichlorophenylphosphine (1.5 mL, 11 mmol) was added in one portion. After stirring for 10 min at –78 °C, the mixture was slowly warmed to room temperature, and stirred for 1.5 h at room temperature. Then the mixture was cooled to –78 °C again, and a suspension of 2-naphthyllithium [prepared from 2-bromonaphthalene (2.69 g, 13 mmol) and 1.7 M t-BuLi solution in pentane (15.2 mL, 26 mmol) in Et_2O (60 mL) at –78 °C] was added via a cannula at –78 °C. The mixture was warmed to room temperature overnight and filtered through a pad of Celite. The filtrate was concentrated, and the residue was purified by chromatography (SiO_2, hexane-EtOAc-Et_3N = 85:10:5) to afford the title compound (4.42 g, 90%) as a mixture of two isomers. The ratio of (R_c, S_{Fe}, S_P)-**5** to (R_c, S_{Fe}, R_P)-**6** is about 5:1. Fractional crystallization from hexane gave (R_c, S_{Fe}, S_P)-**5** (3.10 g, 63%) and (R_c, S_{Fe}, R_P)-**6** (687 mg, 14%). (R_c, S_{Fe}, S_P)-**5** : ^{1}H NMR ($CDCl_3$, 400.13 MHz): δ 1.28 (d, 3H, *J* = 6.2 Hz); 1.80 (s, 6H); 3.90 (br. s, 1H); 3.92 (s, 5H); 4.20 (m, 1H), 4.22 (t, 1H, *J* = 2.2 Hz); 4.38 (br. s, , 1H); 7.18 ~ 7.26 (m, 5H); 7.48 (m, 2H), 7.58 (ddd, 1H, *J* = 8.4, 5.6 and 1.6 Hz); 7.79 (d, 1H, *J* = 8.4 Hz); 7.83 (m, 2H); 8.18 (d, 1H, *J* = 9.5 Hz);. ^{31}P NMR ($CDCl_3$, 162 MHz): δ –20.88. (R_c, S_{Fe}, R_P)-**6** : ^{1}H NMR ($CDCl_3$, 400.13 MHz): δ 1.27 (d, 3H, *J* = 5.7Hz); 1.76 (s, 6H); 3.90 (br. s, 1H); 3.96 (s, 5H); 4.18 (m, 1H), 4.29 (t, 1H, *J* = 2.2 Hz); 4.41 (br. s, , 1H); 7.29 (ddd, 1H, *J* = 8.3, 7.0 and 1.6 Hz); 7.34 (m, 3H); 7.39 (m, 2H); 7.59~7.67 (m, 5H), 7.74 (m, 1H);. ^{31}P NMR ($CDCl_3$, 162 MHz): δ –20.57.

Example 6

(R_c, S_{Fe}, S_P)-2-[(1-N,N-Dimethylamino)ethyl]-1-[(2-naphthyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-5]:



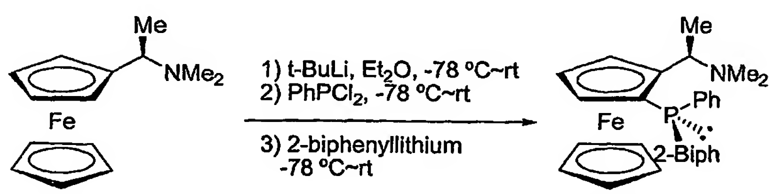
(R)-1 (R_C-S_{Fe}-S_P)-5

To a solution of (R)-N,N-dimethyl-1-ferrocenylethylamine [(R)-Ugi's amine, (R)-1] (2.06 g, 8 mmol) in Et_2O (15 mL) was added 1.5 M t-BuLi solution in pentane (6.0 mL, 9 mmol) over 10 min via a syringe at –78 °C. After addition was completed, the mixture was warmed to room temperature, and stirred for 1.5 h at room temperature. The resulting red solution was cooled to –78 °C again, and dichlorophenylphosphine (1.22 mL, 9 mmol) was added in one portion. After stirring for 10 min at –78 °C, the mixture was slowly warmed to room temperature, and stirred for 1.5 h at room temperature. Then the mixture was cooled to –78 °C again, and a solution of 2-naphthylmagnesium bromide [prepared from 2-bromonaphthalene (2.20 g, 10.6 mmol) and magnesium (258 mg, 10.6 mmol) in Et_2O (20 mL)] was added via a cannula at –78 °C. The mixture was warmed to room temperature overnight. The reaction was quenched with saturated NH_4Cl solution (20 mL). The organic layer was separated, and the aqueous layer was extracted with Et_2O (20 mL). The

combined organic layers were washed with brine (20 mL), dried ($MgSO4$), and concentrated. The residue was purified by chromatography (SiO_2, hexane-EtOAc-Et_3N = 85:10:5) to afford the title compound (3.42 g, 87%) as single diastereomer. ^1H NMR ($CDCl_3$, 400.13 MHz): δ 1.28 (d, 3H, J = 6.2 Hz); 1.80 (s, 6H); 3.90 (br. s, 1H); 3.92 (s, 5H); 4.20 (m, 1H), 4.22 (t, 1H, J = 2.2 Hz); 4.38 (br. s, , 1H); 7.18 ~ 7.26 (m, 5H); 7.48 (m, 2H), 7.58 (ddd, 1H, J = 8.4, 5.6 and 1.6 Hz); 7.79 (d, 1H, J = 8.4 Hz); 7.83 (m, 2H); 8.18 (d, 1H, J = 9.5 Hz);. ^{31}P NMR ($CDCl_3$, 162 MHz): δ –20.88.

Example 7

(R_c, S_{Fe}, S_P)-2-[(1-N,N-Dimethylamino)ethyl]-1-[(2-biphenyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-7]:



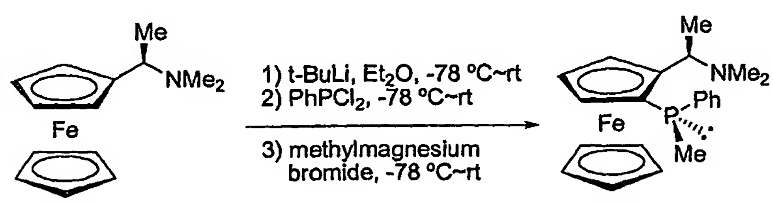
(R)-1 (R_C-S_{Fe}-S_P)-7

To a solution of (R)-N,N-dimethyl-1-ferrocenylethylamine [(R)-Ugi's amine, (R)-1] (2.57 g, 10 mmol) in Et_2O (20 mL) was added 1.5 M t-BuLi solution in pentane (7.33 mL, 11 mmol) over 10 min via a syringe at –78 °C. After addition was completed, the mixture was warmed to room temperature, and stirred for 1.5 h at room temperature. The resulting red solution was cooled to –78 °C again, and dichlorophenylphosphine (1.50 mL, 11 mmol) was added in one

portion. After stirring for 10 min at –78 °C, the mixture was slowly warmed to room temperature, and stirred for 1.5 h at room temperature. Then the mixture was cooled to –78 °C again, and a suspension of 2-biphenyllithium [prepared from 2-bromobiphenyl (2.24 mL, 13 mmol) and 1.5 M t-BuLi solution in pentane (17.3 mL, 26 mmol) in Et_2O (30 mL) at –78 °C] was added via a cannula at –78 °C. The mixture was warmed to room temperature overnight and filtered through a pad of Celite. The filtrate was concentrated, and the residue was purified by chromatography (SiO_2, hexane-EtOAc-Et3N = 85:10:5) to afford the title compound (4.87 g, 94%) as single diastereomer. ^{1}H NMR ($CDCl_3$, 400.13 MHz): δ 1.25 (d, 3H, J = 6.7Hz); 1.85 (s, 6H); 3.69 (s, 5H); 3.76 (m, 1H), 4.17 (m, 1H), 4.29 (t, 1H, J = 2.4 Hz); 4.32 (m, 1H); 7.10 ~ 7.19 (m, 5H); 7.31 (m, 1H), 7.37~7.48 (m, 5H), 7.64 (m, 1H); 7.69 (m, 1H); 7.71 (m, 1H). ^{31}P NMR ($CDCl_3$, 162 MHz): δ –32.96

Example 8

(R_c, S_{Fe}, S_P)-2-[(1-N,N-Dimethylamino)ethyl]-1-(methylphenylphosphino)ferrocene [(R_c, S_{Fe}, R_P)-8]:



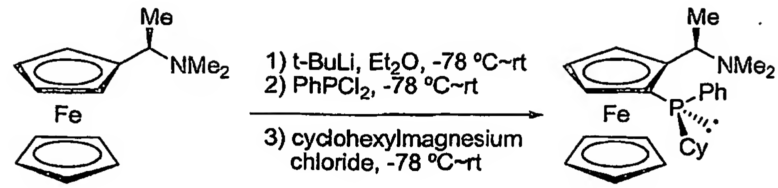
(R)-1

(R_C-S_{Fe}-R_P)-8

To a solution of (R)-N,N-dimethyl-1-ferrocenylethylamine [(R)-Ugi's amine, (R)-**1**] (2.57 g, 10 mmol) in Et_2O (20 mL) was added 1.5 M t-BuLi solution in pentane (7.33 mL, 11 mmol) over 10 min via a syringe at –78 °C. After addition was completed, the mixture was warmed to room temperature, and stirred for 1.5 h at room temperature. The resulting red solution was cooled to –78 °C again, and dichlorophenylphosphine (1.50 mL, 11 mmol) was added in one portion. After stirring for 10 min at –78 °C, the mixture was slowly warmed to room temperature, and stirred for 1.5 h at room temperature. Then the mixture was cooled to –78 °C again, and 3.0 M solution of MeMgBr in Et_2O (4.0 mL, 12 mmol) was added via a syringe at –78 °C. The mixture was warmed to room temperature overnight. The reaction was quenched with saturated NH_4Cl solution (20 mL). The organic layer was separated, and the aqueous layer was extracted with Et_2O (20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), and concentrated. The residue was purified by chromatography (SiO_2, hexane-EtOAc-Et_3N = 85:10:5) to afford the title compound (3.36 g, 89%) as red oil. ^{1}H NMR ($CDCl_3$, 400.13 MHz): δ 1.24 (d, 3H, J = 6.7Hz); 1.56 (d, 3H, J = 4.4 Hz); 1.72 (s, 6H); 4.07 (m, 1H), 4.13 (s, 5H); 4.30 (m, 1H), 4.34 (m, 2H); 7.14 ~ 7.20 (m, 3H); 7.30~7.37 (m, 2H). ^{31}P NMR ($CDCl_3$, 162 MHz): δ –43.47

Example 9

(R_c, S_{Fe}, S_P)-2-[(1-N,N-Dimethylamino)ethyl]-1-(cyclohexylphenylphosphino)ferrocene [(R_c, S_{Fe}, R_P)-9]:



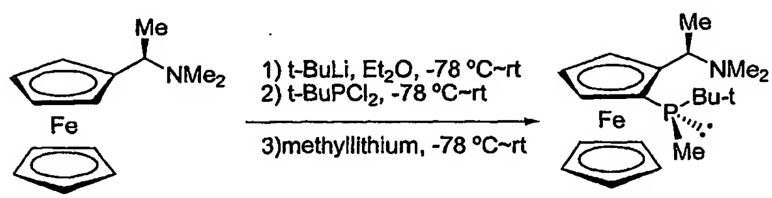
(R)-1 $(R_C\text{-}S_{Fe}\text{-}R_P)$-9

To a solution of (R)-N,N-dimethyl-1-ferrocenylethylamine [(R)-Ugi's amine, (R)-1] (2.57 g, 10 mmol) in Et_2O (20 mL) was added 1.5 M t-BuLi solution in pentane (7.35 mL, 11 mmol) over 10 min via a syringe at –78 °C. After addition was completed, the mixture was warmed to room temperature, and stirred for 1.5 h at room temperature. The resulting red solution was cooled to –78 °C again, and dichlorophenylphosphine (1.50 mL, 11 mmol) was added in one portion. After stirring for 10 min at –78 °C, the mixture was slowly warmed to room temperature, and stirred for 1.5 h at room temperature. Then the mixture was cooled to –78 °C again, and 2.0 M solution of cyclohexymagnesium chloride in Et_2O (6.0 mL, 12 mmol) was added via a syringe at –78 °C. The mixture was warmed to room temperature overnight. The reaction was quenched with saturated NH_4Cl solution (20 mL). The organic layer was separated, and the aqueous layer was extracted with Et_2O (20 mL). The combined organic layers were washed with brine (20 mL), dried ($MgSO_4$), and concentrated. The residue was purified by chromatography (SiO_2, hexane-EtOAc-Et_3N = 90:5:5) to afford the title compound (4.09 g, 92%) as red oil. ^1H NMR ($CDCl_3$, 400.13 MHz): δ 1.16 (d, 3H, J = 6.7Hz); 1.19~2.03 (m, 11H); 1.50 (s, 6H); 3.99(m, 1H), 4.11 (s, 5H); 4.30 (m, 1H), 4.32 (t, 1H, J = 2.5 Hz); 4.37

(m, 1H), 7.12 ~ 7.150 (m, 3H); 7.18~7.23 (m, 2H). ^{31}P NMR ($CDCl_3$, 162 MHz): δ –14.86

Example 10

(R_c, S_{Fe}, S_P)-2-[(1-N,N-Dimethylamino)ethyl]-1-[methyl(*tert*-butyl)phenylphosphino)ferrocene [(R_c, S_{Fe}, R_P)-10]:



(R)-1

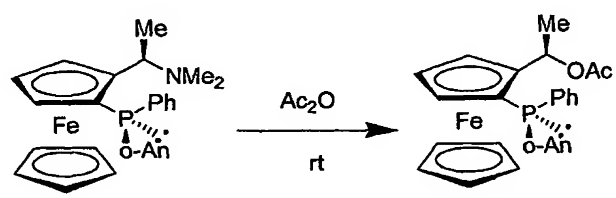
(R_C-S_{Fe}-R_P)-10

To a solution of (R)-N,N-dimethyl-1-ferrocenylethylamine [(R)-Ugi's amine, (R)-1] (1.29 g, 5 mmol) in Et_2O (15 mL) was added 1.5 M t-BuLi solution in pentane (3.7mL, 5.5 mmol) over 10 min via a syringe at –78 °C. After addition was completed, the mixture was warmed to room temperature, and stirred for 1.5 h at room temperature. The resulting red solution was cooled to –78 °C again, and tert-butyldichlorophosphine (875 mg, 5.5 mmol) was added in one portion. After stirring for 10 min at –78 °C, the mixture was slowly warmed to room temperature, and stirred for 1.5 h at room temperature. Then to the mixture a 1.6 M solution of methyllithium in Et_2O (3.75 mL, 6.0 mmol) was added via a syringe at –78 °C. The mixture was warmed to room temperature overnight and filtered through a pad of Celite. The filtrate was concentrated, and the residue

was purified by chromatography (SiO_2, hexane-EtOAc-Et_3N = 90:5:5) to afford the title compound (1.54 g, 86%) as red oil. ^1H NMR ($CDCl_3$, 250.13 MHz): δ 1.09 (d, 9H, J = 12.0 Hz), 1.27 (d, 3H, J = 6.7Hz); 1.45 (d, 3H, J = 3.3 Hz); 2.08 (s, 6H); 3.92 (m, 1H), 4.10 (s, 5H);, 4.28 (m, 3H). ^{31}P NMR ($CDCl_3$, 101 MHz): δ -6.47

Example 11

(R_c, S_{Fe}, S_P)-2-(1-Acetoxyethyl)-1-[(2-methoxyphenyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-11]:

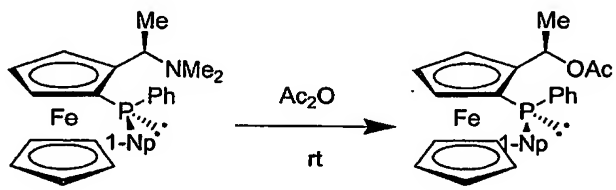


R_C-S_{Fe}-S_P-**2** R_C-S_{Fe}-S_P-**11**

A solution of (R_c, S_{Fe}, S_P)-**2** (1.18 g, 2.5 mmol) in acetic anhydride (10 mL) was stirred for 60 h at room temperature. The excess acetic anhydride was removed under reduced pressure (<1 Torr, <30 °C) to give the title compound (1.21 g, 100%) as yellow solid, which is pure enough for the use in the next reaction. ^1H NMR ($CDCl_3$, 400.13 MHz): δ 1.19 (s, 3H); 1.64 (d, 3H, J = 6.5 Hz); 3.90 (s, 3H); 3.92 (m, 1H); 4.07 (s, 5H); 4.34 (t, 1H, J = 2.6 Hz); 5.55 (m, 1H);6.15 (m, 1H); 6.87 (td, 1H, J = 7.4 and 0.9 Hz); 6.95 (q, 1H, J = 4.8 Hz); 7.08 ~ 7.21 (m, 6H); 7.35 (m, 1H); ^{31}P NMR ($CDCl_3$, 162 MHz): δ –39.30.

Example 12

(R_c, S_{Fe}, S_P)-2-(1-Acetoxyethyl)-1-[(1-naphthyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-12]:



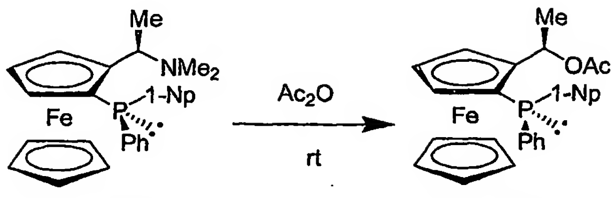
R_C-S_{Fe}-S_P-3 R_C-S_{Fe}-S_P-12

A solution of (R_c, S_{Fe}, S_P)-**3** (1.47 g, 3.0 mmol) in acetic anhydride (20 mL) was stirred for 60 h at room temperature. The excess acetic anhydride was removed under reduced pressure (<1 Torr, <30 °C) to give the title compound (1.52 g, 100%) as yellow solid, which is pure enough for the use in the next reaction. ^{1}H NMR ($CDCl_3$, 400.13 MHz): δ 1.29 (s, 3H); 1.67 (d, 3H, J = 6.5 Hz); 3.72 (s, 5H); 3.94 (m, 1H); 4.35 (t, 1H, J = 2.6 Hz); 4

.57 (m, 1H); 6.28 (m, 1H); 7.13 ~ 7.22 (m, 5H); 7.38~7.43 (m, 2H), 7.53 (ddd, 1H, J = 8.0, 6.7 and 1.1 Hz), 7.64(ddd, 1H, J = 8.4, 6.8 and 1.4 Hz), 7.89 (t, 2H, J = 7.0 Hz); 9.28 (t, 1H, J = 7.0 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz): δ –39.81.

Example 13

(R_c, S_{Fe}, R_P)-2-(1-Acetoxyethyl)-1-[(1-naphthyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, R_P)-13]:

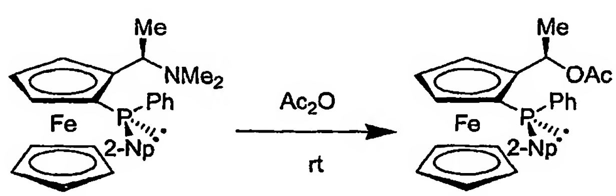


R_C-S_{Fe}-R_P-**4** R_C-S_{Fe}-R_P-**13**

A solution of (R_c, S_{Fe}, R_P)-**4** (1.47 g, 3.0 mmol) in acetic anhydride (20 mL) was stirred for 60 h at room temperature. The excess acetic anhydride was removed under reduced pressure (<1 Torr, <30 °C) to give the title compound (1.52 g, 100%) as yellow solid, which is pure enough for the use in the next reaction. ^{1}H NMR ($CDCl_3$, 400.13 MHz): δ 0.83 (s, 3H); 1.62 (d, 3H, J = 6.5 Hz); 3.83 (m, 1H); 4.10 (s, 5H); 4.40 (t, 1H, J = 2.6 Hz); 5.61 (m, 1H); 6.21 (m, 1H); 7.11 (ddd, 1H, J = 7.0, 4.6 and 1.1 Hz), 7.28 ~ 7.41(m, 6H); 7.55~7.43 (m, 2H), 7.75 (m, 2H), 8.29 (m, 1H); ^{31}P NMR ($CDCl_3$, 162 MHz): δ –31.33.

Example 14

(R_c, S_{Fe}, S_P)-2-(1-Acetoxyethyl)-1-[(2-naphthyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-14]:



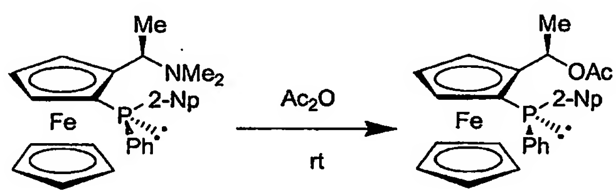
R_C-S_{Fe}-S_P-**5** R_C-S_{Fe}-S_P-**14**

A solution of (R_c, S_{Fe}, S_P)-**5** (1.47 g, 3.0 mmol) in acetic anhydride (20 mL) was stirred for 60 h at room temperature. The excess acetic anhydride was removed

under reduced pressure (<1 Torr, <30 °C) to give the title compound (1.52 g, 100%) as yellow solid, which is pure enough for the use in the next reaction. ^{1}H NMR ($CDCl_3$, 400.13 MHz): δ 1.21 (s, 3H); 1.65 (d, 3H, J = 6.5 Hz); 3.83 (m, 1H); 4.03 (s, 5H); 4.33 (t, 1H, J = 2.6 Hz); 4.57 (m, 1H); 6.24 (m, 1H); 7.19 ~ 7.27(m, 5H); 7.46~7.51 (m, 3H), 7.81 (m, 3H), 8.11 (d, 1H, J = 10.4 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz): δ –22.89.

Example 15

(R_c, S_{Fe}, R_P)-2-(1-Acetoxyethyl)-1-[(2-naphthyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, R_P)-15]:



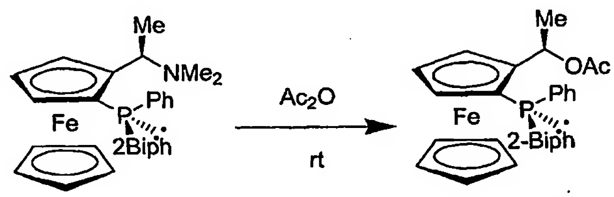
R_C-S_{Fe}-R_P-6 **R_C-S_{Fe}-R_P-15**

A solution of (R_c, S_{Fe}, R_P)-**6** (1.47 g, 3.0 mmol) in acetic anhydride (20 mL) was stirred for 60 h at room temperature. The excess acetic anhydride was removed under reduced pressure (<1 Torr, <30 °C) to give the title compound (1.52 g, 100%) as yellow solid, which is pure enough for the use in the next reaction. ^{1}H NMR ($CDCl_3$, 400.13 MHz): δ 0.92 (s, 3H); 1.64 (d, 3H, J = 6.4 Hz); 3.87 (m, 1H); 4.07 (s, 5H); 4.40 (t, 1H, J = 2.6 Hz); 5.61 (m, 1H); 6.23 (m, 1H); 7.27 (ddd, 1H, J = 8.2, 6.8 and 1.4 Hz), 7.32 ~ 7.38(m, 3H); 7.39~7.44 (m, 2H),

7.53~7.57 (m, 2H), 7.60 (d, 1H, J = 8.0 Hz), 7.69 (m, 2H), 7.74 (m, 1H); ^{31}P NMR ($CDCl_3$, 162 MHz): δ –22.58.

Example 16

(R_c, S_{Fe}, S_P)-2-(1-Acetoxyethyl)-1-[(2-biphenyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-16]:

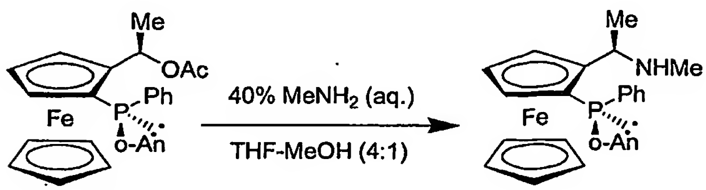


R_C-S_{Fe}-S_P-7 R_C-S_{Fe}-S_P-16

A solution of (R_c, S_{Fe}, S_P)-**7** (1.47 g, 3.0 mmol) in acetic anhydride (20 mL) was stirred for 60 h at room temperature. The excess acetic anhydride was removed under reduced pressure (<1 Torr, <30 °C) to give the title compound (1.52 g, 100%) as yellow solid, which is pure enough for the use in the next reaction. ^1H NMR ($CDCl_3$, 400.13 MHz): δ 1.25 (s, 3H); 1.52 (d, 3H, J = 6.5 Hz); 3.73 (s, 5H); 3.96 (m, 1H); 4.33 (t, 1H, J = 2.6 Hz); 4.48 (m, 1H); 5.81 (m, 1H); 7.16 ~ 7.27(m, 6H); 7.38~7.51 (m, 6H), 7.70~7.73 (m, 2H). ^{31}P NMR ($CDCl_3$, 162 MHz): δ –35.03.

Example 17

(R_c, S_{Fe}, S_P)-2-[(1- N-Methylamino)ethyl]-1-[(2-methoxyphenyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-17]:

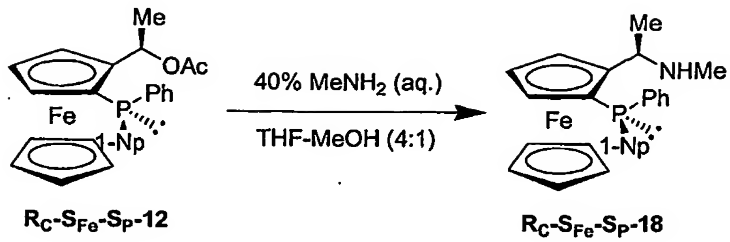


R_C-S_{Fe}-S_P-**11** R_C-S_{Fe}-S_P-**17**

A solution of (R_c, S_{Fe}, S_P)-**11** (1.21 g, 2.5 mmol) and 40% methylamine aqueous solution (6.0 mL) in THF (20 mL) and MeOH (5 mL) was stirred for 3 days at 40 °C, and concentrated. The residue was dissolved in Et_2O (20 mL), washed with brine (10 mL), dried (Na_2SO_4), and evaporated under reduced pressure. The crude product was purified by chromatography (SiO_2, hexane-EtOAc-Et3N = 80:15:5) to give the title compound (1.07 g, 94%) as orange crystals. ^{1}H NMR ($CDCl_3$, 250.13 MHz): δ 1.44 (d, 3H, J = 6.5 Hz); 1.94 (s, 3H); 3.91 (m, 2H); 3.95 (s, 3H); 4.05 (s, 5H); 4.29 (t, 1H, J = 2.5 Hz); 4.46 (m, 1H); 7.90 (dt, 1H, J = 7.3 and 1.0 Hz), 6.97 (ddd, 1H, J = 8.3, 5.0 and 1.0 Hz), 7.15 (ddd, 1H, J = 7.3, 5.5 and 1.8 Hz),7.23 (m, 5H); 7.36 (ddd, 1H, J = 8.3, 7.3 and 1.8 Hz),. ^{31}P NMR ($CDCl_3$, 101 MHz): δ –41.43.

Example 18

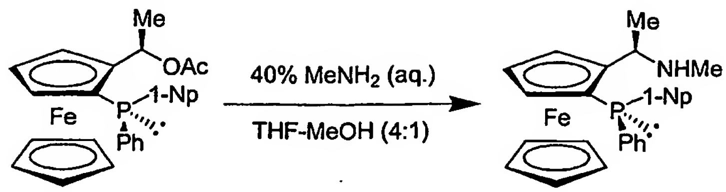
(R_c, S_{Fe}, S_P)-2-[(1- N-Methylamino)ethyl]-1-[(1-naphthyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-18]:



A solution of (R_c, S_{Fe}, S_P)-**12** (633 mg, 1.25 mmol) and 40% methylamine aqueous solution (3.0 mL) in THF (10 mL) and MeOH (2.5 mL) was stirred for 3 days at 40 °C, and concentrated. The residue was dissolved in Et_2O (20 mL), washed with brine (10 mL), dried (Na_2SO_4), and evaporated under reduced pressure. The crude product was purified by chromatography (SiO_2, hexane-EtOAc-Et_3N = 85:10:5) to give the title compound (549 mg, 92%) as orange crystals. ^1H NMR ($CDCl_3$, 400.13 MHz): δ 1.49 (d, 3H, J = 6.6 Hz); 2.07 (s, 3H); 3.69 (s, 5H); 3.95 (m, 1H); 4.01 (m, 1H); 4.31 (t, 1H, J = 2.5 Hz); 4.48 (m, 1H); 7.23 (m, 5H); 7.39 ~ 7.47 (m, 2H); 7.54 (m, 1H); 7.66 (m, 1H); 7.90 (t, 2H, J = 7.9 Hz), 9.25 (dd, 1H, J = 7.9 and 6.7 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ –39.91.

Example 19

(R_c, S_{Fe}, R_P)-2-[(1- N-Methylamino)ethyl]-1-[(1-naphthyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, R_P)-19]:

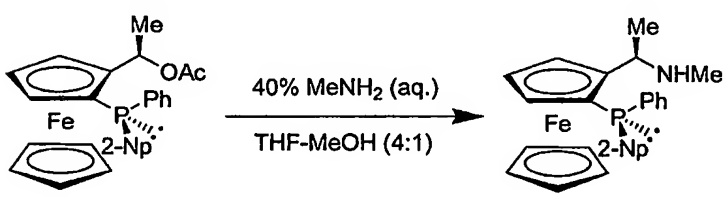


R_C-S_{Fe}-R_P-**13** R_C-S_{Fe}-R_P-**19**

A solution of (R_c, S_{Fe}, R_P)-**7** (633 mg, 1.25 mmol) and 40% methylamine aqueous solution (3.0 mL) in THF (10 mL) and MeOH (2.5 mL) was stirred for 3 days at 40 °C, and concentrated. The residue was dissolved in Et_2O (20 mL), washed with brine (10 mL), dried (Na_2SO_4), and evaporated under reduced pressure. The crude product was purified by chromatography (SiO_2, hexane-EtOAc-Et_3N = 85:10:5) to give the title compound (537 mg, 90%) as orange crystals. ^{1}H NMR ($CDCl_3$, 400.13 MHz): δ 1.45 (d, 3H, J = 6.5 Hz); 1.83 (s, 3H); 3.82 (m, 1H); 3.97 (m, 1H); 4.07 (s, 5H); 3 4.35 (t, 1H, J = 2.5 Hz); 4.53 (m, 1H); 7.20 (m, 1H); 7.30 ~ 7.36 (m, 5H); 7.40 (m, 1H); 7.56 ~ 7.61 (m, 2H); 7.78 (t, 2H, J = 8.2 Hz), 8.38 (m, 1H). ^{31}P NMR ($CDCl_3$, 162 MHz): δ –32.25.

Example 20

(R_c, S_{Fe}, S_P)-2-[(1- N-Methylamino)ethyl]-1-[(2-naphthyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-20]:

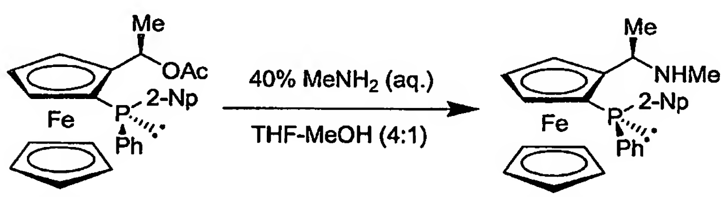


R_C-S_{Fe}-S_P-**14** R_C-S_{Fe}-S_P-**20**

A solution of (R_c, S_{Fe}, S_P)-**14** (633 mg, 1.25 mmol) and 40% methylamine aqueous solution (3.0 mL) in THF (10 mL) and MeOH (2.5 mL) was stirred for 3 days at 40 °C, and concentrated. The residue was dissolved in Et_2O (20 mL), washed with brine (10 mL), dried (Na_2SO_4), and evaporated under reduced pressure. The crude product was purified by chromatography (SiO_2, hexane-EtOAc-Et3N = 85:10:5) to give the title compound (513 mg, 86%) as orange crystals. ^{1}H NMR ($CDCl_3$, 400.13 MHz): δ 1.47 (d, 3H, J = 6.7 Hz); 1.98 (s, 3H); 3.82 (m, 1H); 3.98 (m, 1H); 4.02 (s, 5H); 4.27 (t, 1H, J = 2.5 Hz); 4.47 (m, 1H); 7.27~7.34 (m, 5H); 7.50 (m, 2H); 7.55 (m, 1H); 7.83 (m, 3H); 8.12 (d, 1H, J = 10.0 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ –22.68.

Example 21

(R_c, S_{Fe}, R_P)-2-[(1- N-Methylamino)ethyl]-1-[(2-naphthyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, R_P)-21]:



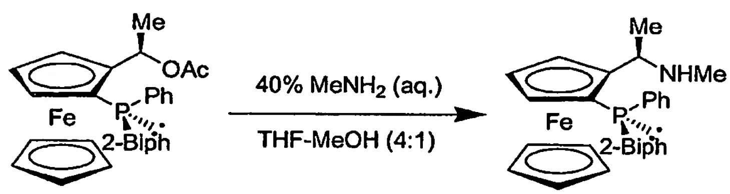
R_C-S_{Fe}-R_P**15** R_C-S_{Fe}-R_P-**21**

A solution of (R_c, S_{Fe}, R_P)-**15** (633 mg, 1.25 mmol) and 40% methylamine aqueous solution (3.0 mL) in THF (10 mL) and MeOH (2.5 mL) was stirred for 3 days at room temperature, and concentrated. The residue was dissolved in Et_2O (20 mL), washed with brine (10 mL), dried (Na_2SO_4), and evaporated under reduced pressure. The crude product was purified by chromatography

(SiO_2, hexane-EtOAc-Et_3N = 85:10:5) to give the title compound (537 mg, 90%) as orange crystals.

Example 22

(R_c, S_{Fe}, S_P)-2-[(1- N-Methylamino)ethyl]-1-[(2-biphenyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-22]:

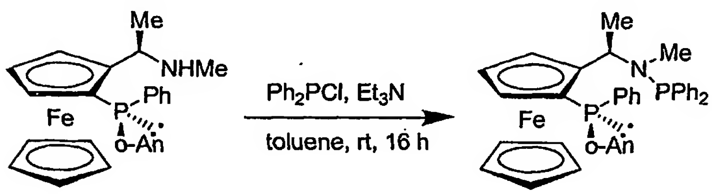


R_C-S_{Fe}-S_P-16 **R_C-S_{Fe}-S_P-22**

A solution of (R_c, S_{Fe}, S_P)-**16** (1.063 g, 2 mmol) and 40% methylamine aqueous solution (5.0 mL) in THF (10 mL) and MeOH (2.5 mL) was stirred for 2 days at 40 °C, and concentrated. The residue was dissolved in Et_2O (20 mL), washed with brine (10 mL), dried (Na_2SO_4), and evaporated under reduced pressure. The residue was recrystallized from hexane to give the title compound (621 mg, 62%) as orange crystals. ^1H NMR ($CDCl_3$, 400.13 MHz): δ 1.34 (d, 3H, J = 6.6 Hz); 1.93 (s, 3H); 3.60 (m, 1H); 3.74 (s, 5H); 4.08 (m, 1H); 4.30 (t, 1H, J = 2.5 Hz); 4.39 (m, 1H); 7.19~7.24 (m, 5H); 7.31 (m, 1H); 7.38~7.50 (m, 5H), 7.59 (ddt, 1H, J = 7.6, 3.5 and 1.0 Hz); 7.67 (m, 2H). ^{31}P NMR ($CDCl_3$, 162 MHz): δ –34.29.

Example 23

(R_c, S_{Fe}, S_P)-2-[1-[(N-Methyl-N-diphenylphosphino)amino]ethyl]-1-[(2-methoxyphenyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-23]:

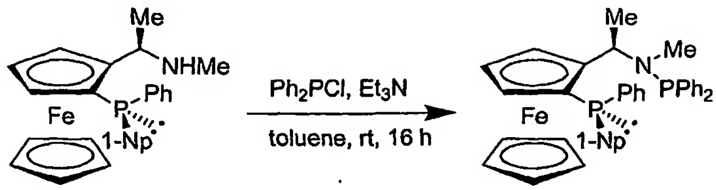


R_C-S_{Fe}-S_P-17 R_C-S_{Fe}-S_P-23

To a solution of (R_c, S_{Fe}, S_P)-**17** (457 mg, 1.0 mmol) and Et3N (0.28 mL, 2.0 mmol) in toluene (2.5 mL) was added dropwise chlorodiphenylphosphine (188 uL, 1.05 mmol) at 0 °C. Then the mixture was warmed to room temperature, and stirred overnight (16 h) at room temperature, and filtered through a pad of neutral aluminium oxide and eluted with hexane-EtOAc (9:1) to afford the title compound (570 mg, 89%) as orange foam. ^1H NMR ($CDCl_3$, 400.13 MHz): δ 1.55 (d, 3H, J = 6.9 Hz); 2.17 (d, 3H, J = 3.4 Hz); 3.87 (s, 8H, overlap); 4.24 (m, 1H); 4.38 (t, 1H, J = 2.4 Hz); 4.53 (m, 1H); 4.88 (m, 1H); 6.88 ~ 6.96 (m, 6H); 7.03 ~ 7.14 (m, 6H); 7.20 ~ 7.37 (m, 7H). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 56.93, –38.64.

Example 24

(R_c, S_{Fe}, S_P)-2-[1-[(N-Methyl-N-diphenylphosphino)amino]ethyl]-1-[(1-naphthyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-24]:

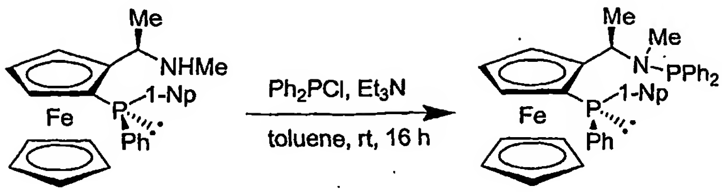


R_C-S_{Fe}-S_P-18 **R_C-S_{Fe}-S_P-24**

To a solution of (R_c, S_{Fe}, S_P)-**18** (477 mg, 1.0 mmol) and Et_3N (0.28 mL, 2.0 mmol) in toluene (2.5 mL) was added dropwise chlorodiphenylphosphine (188 uL, 1.05 mmol) at 0 °C. Then the mixture was warmed to room temperature, and stirred overnight (16 h) at room temperature, and filtered through a pad of neutral aluminium oxide and eluted with hexane-EtOAc (9:1) to afford the title compound (595 mg, 90%) as orange foam. ^{1}H NMR ($CDCl_3$, 400.13 MHz): δ 1.53 (d, 3H, J = 6.8 Hz); 2.22 (d, 3H, J = 3.3 Hz); 3.44 (s, 5H); 4.26 (m, 1H); 4.39 (t, 1H, J = 2.4 Hz); 4.50 (m, 1H); 5.03 (m, 1H); 6.85 ~ 6.94 (m, 4H); 7.04 (tt, 1H, J = 7.2 and 1.4 Hz); 7.09 ~ 7.19 (m, 4H); 7.27 ~ 7.31 (m, 4H); 7.37 ~ 7.43 (m, 3H); 7.48 ~ 7.56 (m, 2H); 7.68 (m, 1H); 7.89 (dd, 2H, J = 8.1 and 4.8 Hz); 9.44 (t, 1H, J = 7.6 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 59.59, –41.03.

Example 25

(R_c, S_{Fe}, R_P)-2-[1-[(N-Methyl-N-diphenylphosphino)amino]ethyl]-1-[(1-naphthyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, R_P)-25]:

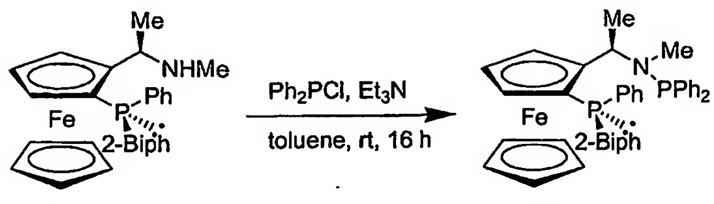


R_C-S_{Fe}-R_P-**19** R_C-S_{Fe}-R_P-**25**

To a solution of (R_c, S_{Fe}, R_P)-**19** (239 mg, 0.5 mmol) and Et_3N (0.14 mL, 1.0 mmol) in toluene (2.0 mL) was added dropwise chlorodiphenylphosphine (89 uL, 0.50 mmol) at 0 °C. Then the mixture was warmed to room temperature, and stirred overnight (16 h) at room temperature, and filtered through a pad of neutral aluminium oxide and eluted with hexane-EtOAc (9:1) to afford the title compound (304 mg, 92%) as orange foam. ^{1}H NMR ($CDCl_3$, 400.13 MHz): δ 1.51 (d, 3H, J = 6.8 Hz); 2.08 (d, 3H, J = 3.5 Hz); 3.90 (s, 5H); 4.15 (m, 1H); 4.44 (t, 1H, J = 2.4 Hz); 4.58 (m, 1H); 5.02 (m, 1H); 6.44 (td, 2H, J = 8.0 and 1.8 Hz); 6.62 (td, 2H, J = 8.0 and 1.2 Hz); 6.80 (tt, 1H, J = 7.4 and 1.2 Hz); 7.20 (m, 1H); 7.15 ~ 7.30 (m, H); 7.58 ~ 7.64 (m, H); 7.70 (dd, 1H, J = 6.8 and 1.8 Hz); 7.79 (d, 1H, J = 8.0 Hz); 8.20 (dd, 1H, J = 8.2 and 2.4 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 58.81, –31.16.

Example 26

(R_c, S_{Fe}, S_P)-2-[1-[(N-Methyl-N-diphenylphosphino)amino]ethyl]-1-[(2-biphenyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-26]:

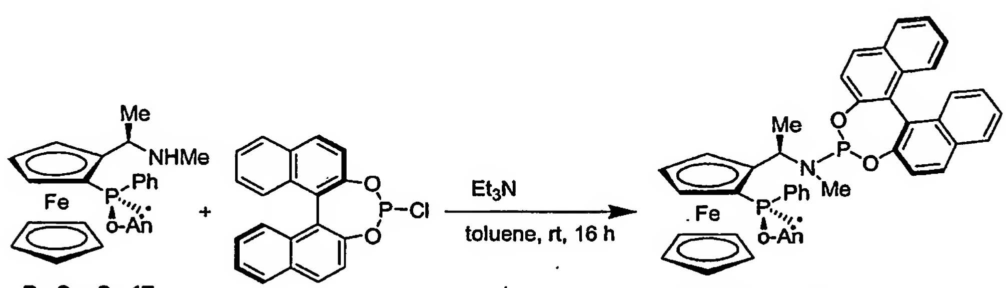


R_C-S_{Fe}-S_P-**22** R_C-S_{Fe}-S_P-**26**

To a solution of (R_c, S_{Fe}, S_P)-**22** (XX mg, 1.0 mmol) and Et_3N (0.28 mL, 2.0 mmol) in toluene (2.5 mL) was added dropwise chlorodiphenylphosphine (188 uL, 1.05 mmol) at 0 °C. Then the mixture was warmed to room temperature, and stirred overnight (16 h) at room temperature, and filtered through a pad of neutral aluminium oxide and eluted with hexane-EtOAc (9:1) to afford the title compound (XX mg, X%) as orange foam. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.50 (d, 3H, J = 6.6 Hz); 2.16 (d, 3H, J = 3.0 Hz); 3.68 (s, 5H); 4.08 (m, 1H); 4.33 (m, 1H); 4.42 (m, 2H); 4.56 (m, 1H); 6.98~7.75 (m, 24H). ^{31}P NMR ($CDCl_3$, 101 MHz): δ 50.70, –35.51.

Example 27

(R_c, S_{Fe}, S_P,R_a)-27:

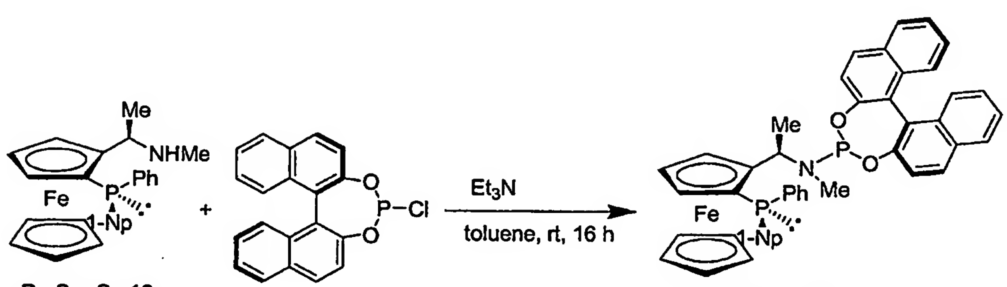


R_C-S_{Fe}-S_P-**17** R_C-S_{Fe}-S_P, R_a-**27**

To a solution of (R_c, S_{Fe}, S_P)-**17** (229 mg, 0.5 mmol) and Et_3N (209 uL, 1.5 mmol) in toluene (4 mL) was added (R)-4-chloro-3,5-dioxa-4-phosphacyclohepta[2,1-a:3,4-a']binaphthalene (175 mg, 0.5 mmol) at 0 °C. Then the mixture was warmed to room temperature, and stirred overnight (16 h) at room temperature, and filtered through a pad of neutral aluminium oxide and eluted with hexane-EtOAc (9:1) to afford the title compound (359 mg, 93%) as orange foam. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.73 (d, 3H, J = 3.5 Hz); 1.79 (d, 3H, J = 7.0 Hz); 3.71 (s, 3H), 3.80 (m, 1H); 4.00 (s, 5H); 4.31 (t, 1H, J = 2.3 Hz); 4.46 (m, 1H); 5.34 (m, 1H); 6.60 (ddd, 1H, J = 7.5, 4.5 and 1.8 Hz), 6.72 (t, 1H, J = 7.5 Hz), 6.82 (dd, 1H, J = 8.8 and 0.8 Hz), 6.91 (ddd, 1H, J = 8.8, 4.5 and 0.8 Hz), 7.15~7.38 (m, 11H), 7.58 (m, 2H), 7.77~7.87 (m, 4H). ^{31}P NMR ($CDCl_3$, 101 MHz): δ 148.51 (d, J = 53.4 Hz); –35.37 (d, J = 53.4 Hz).

Example 28

(R_c, S_{Fe}, S_P,R_a)-28:



R_C-S_{Fe}-S_P-18

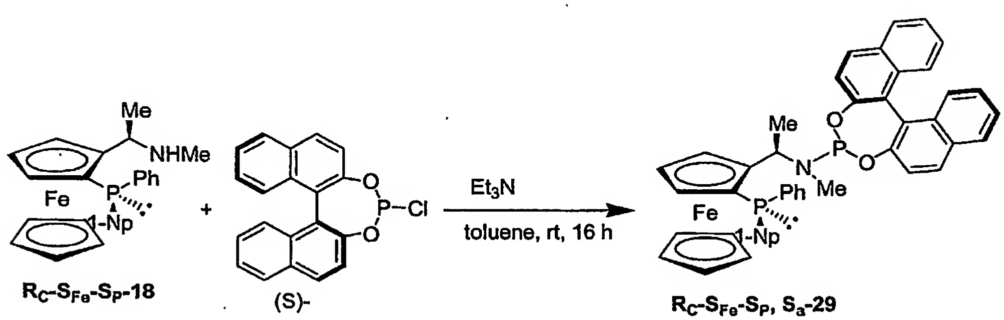
R_C-S_{Fe}-S_P, R_a-28

To a solution of (R_c, S_{Fe}, S_P)-**18**(239 mg, 0.5 mmol) and Et_3N (209 uL, 1.5 mmol) in toluene (4 mL) was added (R)-4-chloro-3,5-dioxa-4-

phosphacyclohepta[2,1-a:3,4-a']binaphthalene (175 mg, 0.5 mmol) at 0 °C. Then the mixture was warmed to room temperature, and stirred overnight (16 h) at room temperature, and filtered through a pad of neutral aluminium oxide and eluted with hexane-EtOAc (9:1) to afford the title compound (376 mg, 95%) as orange foam. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 0.87 (d, 3H, J = 7.0 Hz); 1.82 (d, 3H, J = 3.5 Hz); 3.62 (s, 5H); 4.06 (m, 1H); 4.33 (t, 1H, J = 2.3 Hz); 4.46 (m, 1H); 5.43 (m, 1H); 6.69 (dd, 1H, J = 8.8 and 0.8 Hz), 7.07~7.93 (m, 22H), 9.39 (m, 1H). ^{31}P NMR ($CDCl_3$, 101 MHz): δ 148.37 (d, J = 61.8 Hz); –41.59 (d, J = 61.8 Hz).

Example 29

(R_c, S_{Fe}, S_P,S_a)-29:

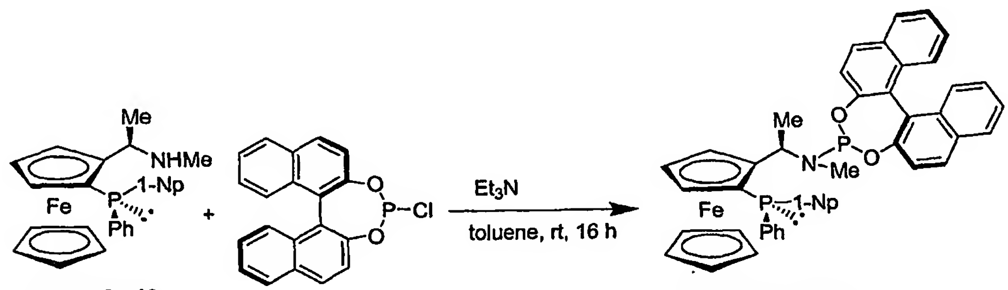


To a solution of (R_c, S_{Fe}, S_P)-**18**(239 mg, 0.5 mmol) and Et_3N (209 uL, 1.5 mmol) in toluene (4 mL) was added (S)-4-chloro-3,5-dioxa-4-phosphacyclohepta[2,1-a:3,4-a']binaphthalene (175 mg, 0.5 mmol) at 0 °C. Then the mixture was warmed to room temperature, and stirred overnight (16 h) at room temperature, and filtered through a pad of neutral aluminium oxide and eluted with hexane-EtOAc (9:1) to afford the title compound (373 mg, 95%) as

orange foam. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.71 (d, 3H, J = 7.0 Hz); 1.99 (d, 3H, J = 3.3 Hz); 3.51 (s, 5H); 4.27 (m, 1H); 4.42 (t, 1H, J = 2.3 Hz); 4.51 (m, 1H); 5.28 (m, 1H); 5.98 (d, 1H, J = 8.5 Hz), 7.10~7.95 (m, 22H), 9.42 (m, 1H). ^{31}P NMR ($CDCl_3$, 101 MHz): δ 150.23 (d, J = 34.3 Hz); –44.84 (d, J = 34.3 Hz).

Example 30

(R_c, S_{Fe}, R_P,R_a)-30:



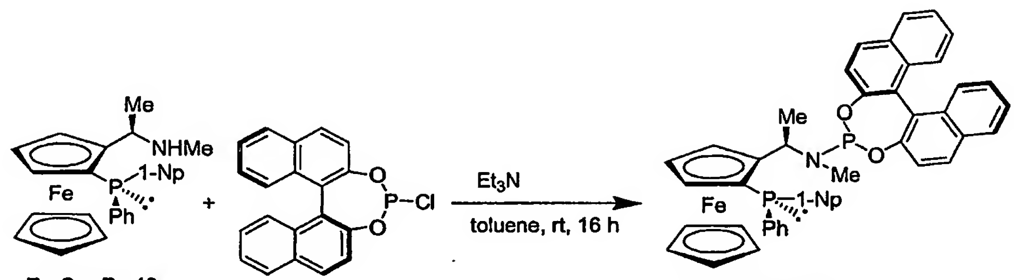
R_C-S_{Fe}-R_P-19 R_C-S_{Fe}-R_P, R_a-30

To a solution of (R_c, S_{Fe}, R_P)-**19**(239 mg, 0.5 mmol) and Et_3N (209 uL, 1.5 mmol) in toluene (4 mL) was added (R)-4-chloro-3,5-dioxa-4-phosphacyclohepta[2,1-a:3,4-a']binaphthalene (175 mg, 0.5 mmol) at 0 °C. Then the mixture was warmed to room temperature, and stirred overnight (16 h) at room temperature, and filtered through a pad of neutral aluminium oxide and eluted with hexane-EtOAc (9:1) to afford the title compound (371 mg, 95%) as orange foam. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.64 (d, 3H, J = 3.5 Hz); 1.79 (d, 3H, J = 7.0 Hz); 4.88 (m, 1H); 4.07 (s, 5H); 4.38 (t, 1H, J = 2.3 Hz); 4.52 (m, 1H); 4.91 (dd, 1H, J = 8.5 and 0.8 Hz), 5.37 (m, 1H); 6.91 (m, 1H); 7.10~7.90

(m, 21H), 8.44 (m, 1H). ^{31}P NMR ($CDCl_3$, 101 MHz): δ 148.18 (d, J = 54.5 Hz); –32.43 (d, J = 54.5 Hz).

Example 31

(R_c, S_{Fe}, R_P,S_a)-31:

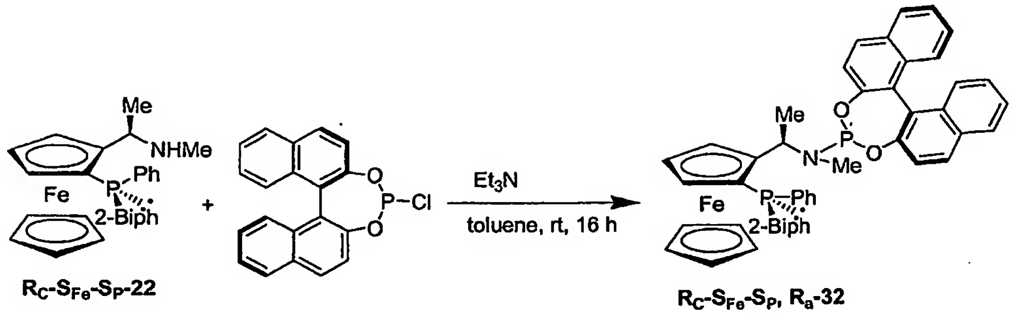


R_C-S_{Fe}-R_P-**19** (S)- R_C-S_{Fe}-R_P, S_a-**31**

To a solution of (R_c, S_{Fe}, R_P)-**19**(239 mg, 0.5 mmol) and Et_3N (209 uL, 1.5 mmol) in toluene (4 mL) was added (S)-4-chloro-3,5-dioxa-4-phosphacyclohepta[2,1-a:3,4-a']binaphthalene (175 mg, 0.5 mmol) at 0 °C. Then the mixture was warmed to room temperature, and stirred overnight (16 h) at room temperature, and filtered through a pad of neutral aluminium oxide and eluted with hexane-EtOAc (9:1) to afford the title compound (377 mg, 95%) as orange foam. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.69 (d, 3H, J = 6.8 Hz); 1.86 (d, 3H, J = 3.5 Hz); 3.97 (s, 5H); 4.07 (m, 1H); 4.43 (t, 1H, J = 2.3 Hz); 4.58 (m, 1H); 5.15 (m, 1H); 5.88 (dd, 1H, J = 8.5 and 0.8 Hz), 6.91 (m, 1H); 7.10~7.92 (m, 22H), 8.31 (m, 1H). ^{31}P NMR ($CDCl_3$, 101 MHz): δ 150.64 (d, J = 21.8 Hz); –33.31 (d, J = 21.8 Hz).

Example 32

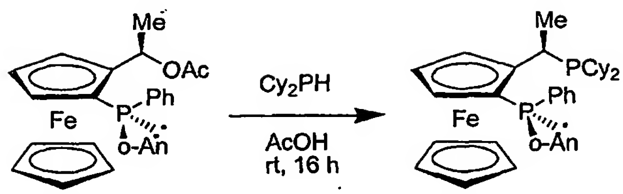
(R_c, S_{Fe}, S_P,R_a)-32:



To a solution of (R_c, S_{Fe}, S_P)-**22**(252 mg, 0.5 mmol) and Et_3N (209 uL, 1.5 mmol) in toluene (4 mL) was added (R)-4-chloro-3,5-dioxa-4-phosphacyclohepta[2,1-a:3,4-a']binaphthalene (175 mg, 0.5 mmol) at 0 °C. Then the mixture was warmed to room temperature, and stirred overnight (16 h) at room temperature, and filtered through a pad of neutral aluminium oxide and eluted with hexane-EtOAc (9:1) to afford the title compound (392 mg, 96%) as orange foam. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.63 (d, 3H, J = 7.0 Hz); 1.76 (d, 3H, J = 3.5 Hz); 3.69 (s, 5H); 4.09 (m, 1H); 4.30 (t, 1H, J = 2.3 Hz); 4.34 (m, 1H); 4.89 (m, 1H); 6.71 (dd, 1H, J = 8.5 and 0.8 Hz), 7.07~7.84 (m, 25 H). ^{31}P NMR ($CDCl_3$, 101 MHz): δ 149.07 (d, J = 60.5 Hz); –36.59 (d, J = 60.5Hz).

Example 33

(R_c, S_{Fe}, S_P)-2-(1-Dicyclohexylphosphino)ethyl]-1-[(2-methoxyphenyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-33]:

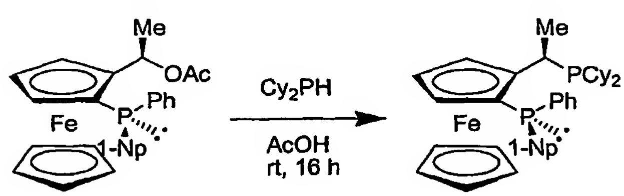


R_C-S_{Fe}-S_P-**11** R_C-S_{Fe}-S_P-**33**

A solution of (R_c, S_{Fe}, S_P)-**11** (486 mg, 1.0 mmol) and dicyclohexylphosphine (243 uL, 1.2 mmol) in acetic acid (3 mL) was stirred overnight at room temperature, and poured into 10% K_2CO_3 aqueous solution (60 mL) with stirring, extracted with Et_2O (2×25 mL). The combined ether layers were dried ($MgSO_4$) and concentrated. The residue was purified by chromatography (SiO_2, hexane-EtOAc = 9:1) to afford the title compound (601 mg, 96%) as orange crystals. ^1H NMR ($CDCl_3$, 250.13 MHz): δ 1.08~1.68 (m, 25 H), 3.12 (m, 1H), 3.91 (s, 5H), 4.07 (m, 1H), 4.29 (t, 1H, J = 2.3 Hz); 4.38 (m, 1H), 6.87~6.98 (m, 2H), 7.15~7.25 (m, 6 H), 7.35 (t, 1 H, J = 7.3 Hz); ^{31}P NMR ($CDCl_3$, 101.25 MHz): δ 15.58 (d, J = 23.2 Hz); -42.23 (d, J = 23.2 Hz).

Example 34

(R_c, S_{Fe}, S_P)-2-(1-Dicyclohexylphosphino)ethyl]-1-[(1-naphthyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-34]:

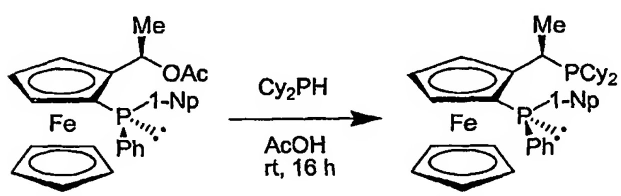


R_C-S_{Fe}-S_P-**12** R_C-S_{Fe}-S_P-**34**

A solution of (R_c, S_{Fe}, S_P)-**12** (506 mg, 1.0 mmol) and dicyclohexylphosphine (243 uL, 1.2 mmol) in acetic acid (3 mL) was stirred overnight at room temperature, and poured into 10% K_2CO_3 aqueous solution (60 mL) with stirring, extracted with Et_2O (2×25 mL). The combined ether layers were dried ($MgSO_4$) and concentrated. The residue was purified by chromatography (SiO_2, hexane-EtOAc = 9:1) to afford the title compound (613 mg, 95%) as orange crystals. ^{1}H NMR ($CDCl_3$, 400.13 MHz): δ 1.14 ~1.57 (m, 25 H); 3.22 (m, 1H); 3.40 (s, 5H); 4.08 (m, 1H); 4.23 (t, 1H, J = 2.4 Hz); 4.31 (m, 1H); 7.16 ~ 7.22 (m, 5H); 7.36 (dd, 1H, J = 8.0 and 7.2 Hz); 7.45 ~ 7.49 (m, 2H); 7.60 (ddd, 1H, J = 8.5, 6.8 and 1.4 Hz); 7.82 (t, 2H, J = 8.1 Hz); 9.28 (dd, 1H, J = 7.6 and 6.8 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ 17.46 (d, J = 27.7 Hz); –42.43 (d, J = 27.7 Hz).

Example 35

(R_c, S_{Fe}, R_P)-2-(1-Dicyclohexylphosphino)ethyl]-1-[(1-naphthyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, R_P)-35]:

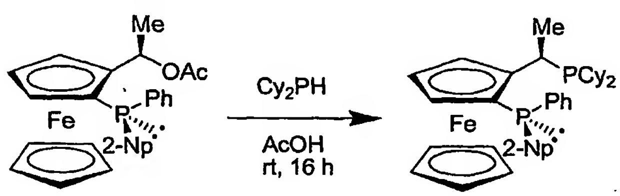


R_C-S_{Fe}-R_P-13 R_C-S_{Fe}-R_P-35

A solution of (R_c, S_{Fe}, S_P)-**13** (506 mg, 1.0 mmol) and dicyclohexylphosphine (243 uL, 1.2 mmol) in acetic acid (3 mL) was stirred overnight at room temperature, and poured into 10% K_2CO_3 aqueous solution (60 mL) with stirring, extracted with Et_2O (2×25 mL). The combined ether layers were dried ($MgSO_4$) and concentrated. The residue was purified by chromatography (SiO_2, hexane-EtOAc = 9:1) to afford the title compound (618 mg, 95%) as orange crystals. ^{1}H NMR ($CDCl_3$, 250.13 MHz): δ 0.84~1.85 (m, 25 H), 3.16 (m, 1H), 3.96 (s, 5H), 4.00 (m, 1H), 4.35 (t, 1H, J = 2.3 Hz); 4.41 (m, 1H), 7.29~7.40 (m, 7H), 7.62~7.79 (m, 4 H), 8.33 (m, 1H); ^{31}P NMR ($CDCl_3$, 101.25 MHz): δ 14.93 (d, J = 22.8 Hz); -34.80 (d, J = 22.8 Hz).

Example 36

(R_c, S_{Fe}, S_P)-2-(1-Dicyclohexylphosphino)ethyl]-1-[(2-naphthyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-36]:



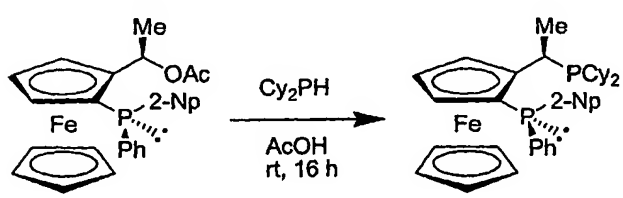
R_C-S_{Fe}-S_P-14 **R_C-S_{Fe}-S_P-36**

A solution of (R_c, S_{Fe}, S_P)-**14** (506 mg, 1.0 mmol) and dicyclohexylphosphine (243 uL, 1.2 mmol) in acetic acid (3 mL) was stirred overnight at room temperature, and poured into 10% K_2CO_3 aqueous solution (60 mL) with stirring, extracted with Et_2O (2×25 mL). The combined ether layers were dried

($MgSO_4$) and concentrated. The residue was purified by chromatography (SiO_2, hexane-EtOAc = 9:1) to afford the title compound (599 mg, 93%) as orange crystals. ^{1}H NMR ($CDCl_3$, 250.13 MHz): δ 1.15~1.71 (m, 25 H), 3.26 (m, 1H), 3.79 (s, 5H), 4.10 (m, 1H), 4.29 (t, 1H, J = 2.3 Hz); 4.37 (m, 1H), 7.17~7.24 (m, 5H), 7.34 (m, 1 H), 7.50 (d, 1H, J = 9.5 Hz); 7.50 (dd, 1H, J = 3.0 and 1.5 Hz); 7.57 (ddd, 1H, J = 8.3, 5.0 and 1.5 Hz); 7.81 (d, 1H, J = 8.5 Hz); 7.87 (m, 1H), 8.31 (d, 1H, J = 9.5 Hz); ^{31}P NMR ($CDCl_3$, 101.25 MHz): δ 15.67 (d, J = 30.9 Hz); -34.20 (d, J = 30.9Hz).

Example 37

(R_c, S_{Fe}, R_P)-2-(1-Dicyclohexylphosphino)ethyl]-1-[(2-naphthyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, R_P)-37]:



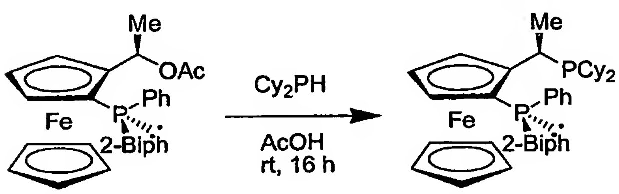
R_C-S_{Fe}-R_P-15 R_C-S_{Fe}-R_P-37

A solution of (R_c, S_{Fe}, S_P)-**15** (506 mg, 1.0 mmol) and dicyclohexylphosphine (243 uL, 1.2 mmol) in acetic acid (3 mL) was stirred overnight at room temperature, and poured into 10% K_2CO_3 aqueous solution (60 mL) with stirring, extracted with Et_2O (2×25 mL). The combined ether layers were dried ($MgSO_4$) and concentrated. The residue was purified by chromatography (SiO_2,

hexane-EtOAc = 9:1) to afford the title compound (608 mg, 94%) as orange crystals. ^{1}H NMR ($CDCl_3$, 250.13 MHz): δ 1.07~1.68 (m, 25 H), 3.26 (m, 1H), 3.85 (s, 5H), 4.07 (m, 1H), 4.34 (t, 1H, J = 2.3 Hz); 4.40 (m, 1H), 7.30~7.77 (m, 12H); ^{31}P NMR ($CDCl_3$, 101.25 MHz): δ 15.56 (d, J = 33.1 Hz); -25.12 (d, J = 33.1 Hz).

Example 38

(R_c, S_{Fe}, S_P)-2-(1-Dicyclohexylphosphino)ethyl]-1-[(2-biphenyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-38]:



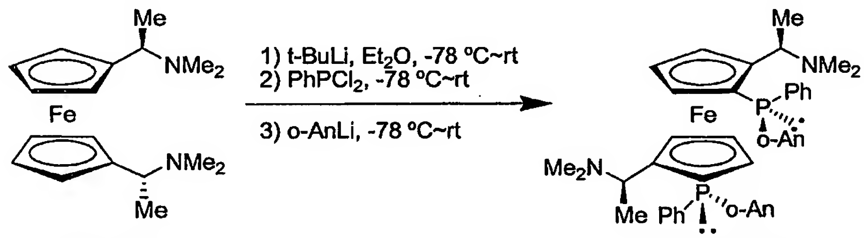
R_C-S_{Fe}-S_P-**16** R_C-S_{Fe}-S_P-**38**

A solution of (R_c, S_{Fe}, S_P)-**16** (531 mg, 1.0 mmol) and dicyclohexylphosphine (243 uL, 1.2 mmol) in acetic acid (3 mL) was stirred overnight at room temperature, and poured into 10% K_2CO_3 aqueous solution (60 mL) with stirring, extracted with Et_2O (2×25 mL). The combined ether layers were dried ($MgSO_4$) and concentrated. The residue was purified by chromatography (SiO_2, hexane-EtOAc = 9:1) to afford the title compound (650 mg, 97%) as orange crystals. ^{1}H NMR ($CDCl_3$, 250.13 MHz): δ 1.02~1.72 (m, 25 H), 2.93 (m, 1H), 3.66 (s, 5H), 3.76 (m, 1H), 4.29 (t, 1H, J = 2.3 Hz); 4.32 (m, 1H), 7.14~7.69 (m,

14 H); ^{31}P NMR ($CDCl_3$, 101.25 MHz): δ 18.44 (d, J = 36.7 Hz); -37.67 (d, J = 36.7 Hz).

Example 39

(R_c, S_{Fe}, S_P)-2,2'-Bis[(1-N,N-dimethylamino)ethyl]-1,1'-bis[(2-methoxyphenyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-40]:



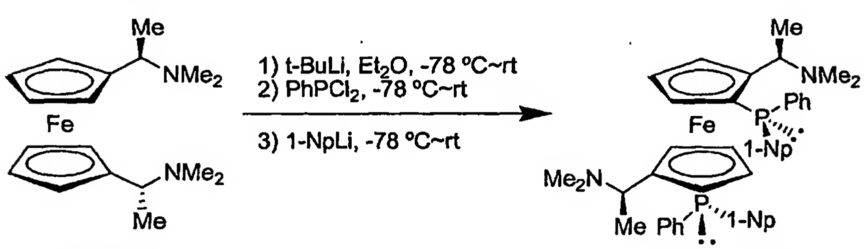
(R,R)-39 **Rc-SFe-Sp-40**

To a solution of (R,R)-1,1'-bis(1-N,N-dimethylaminoethyl)ferrocene [(R,R)-**20**] (986 mg, 3.0 mmol) in Et_2O (30 mL) was added 1.5 M t-BuLi solution in pentane (6.0 mL, 9 mmol) over 10 min via a syringe at –78 °C. After addition was completed, the mixture was warmed to room temperature, and stirred for 1.5 h at room temperature. The resulting red solution was cooled to –78 °C again, and dichlorophenylphosphine (1.22 mL, 9.0 mmol) was added in one portion. After stirring for 10 min at –78 °C, the mixture was slowly warmed to room temperature, and stirred for 1.5 h at room temperature. The mixture was then cooled to –78 °C again, and a solution of (2-methoxy)phenyllithium [prepared from 2-bromoanisole (1.87 g, 10 mmol) and 1.5 M t-BuLi solution in pentane

(13.3 mL, 20 mmol) in Et_2O (50 mL) at –78 °C] was added slowly via a cannula. The mixture was warmed to room temperature overnight, and filtered through a pad of Celite. The filtrate was concentrated. The residue was purified by chromatography (SiO_2, hexane-EtOAc-Et_3N = 80:15:5) to afford the title compound (1.10 g, 48%) as yellow foam. ^1H NMR ($CDCl_3$, 400.13 MHz): δ 1.28 (d, 6H, J = 6.7 Hz); 1.71 (s, 12H); 3.16 (m, 2H); 3.84 (s, 6H); 4.05 (m, 2H); 4.16 (m, 2H); 4.53 (t, 2H, J = 2.3 Hz); 6.62 (t, 2H, J = 7.4 Hz); 6.73 (dd, 2H, J = 8.1 and 4.6 Hz); 6.85 (ddd, 2H, J = 7.4, 5.3 and 1.8 Hz); 7.03 ~ 7.11 (m, 10H); 7.17 (td, 2H, J = 8.5 and 1.6 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz): δ –39.53 (s).

Example 40

(R_c, S_{Fe}, S_P)-2,2'-Bis[(1-N,N-dimethylamino)ethyl]-1,1'-bis[(1-naphthyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-41]:



(R,R)-20

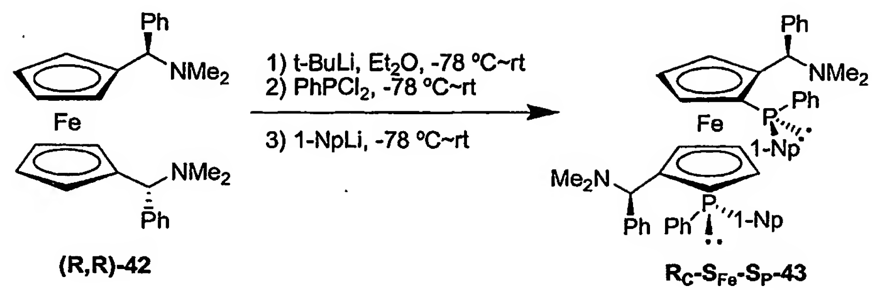
R_C-S_{Fe}-S_P-41

To a solution of (R,R)-1,1'-bis(1-N,N-dimethylaminoethyl)ferrocene [(R,R)-20] (986 mg, 3.0 mmol) in Et_2O (30 mL) was added 1.5 M t-BuLi solution in pentane (6.0 mL, 9 mmol) over 10 min via a syringe at –78 °C. After addition was completed, the mixture was warmed to room temperature, and stirred for 1.5 h

at room temperature. The resulting red solution was cooled to –78 °C again, and dichlorophenylphosphine (1.22 mL, 9.0 mmol) was added in one portion. After stirring for 10 min at –78 °C, the mixture was slowly warmed to room temperature, and stirred for 1.5 h at room temperature. The mixture was then cooled to –78 °C again, and a solution of 1-naphthyllithium [prepared from 1-bromonaphthalene (2.07 g, 10 mmol) and 1.5 M t-BuLi solution in pentane (13.3 mL, 20 mmol) in Et_2O (50 mL) at –78 °C] was added slowly via a cannula. The mixture was warmed to room temperature overnight, and filtered through a pad of Celite. The filtrate was concentrated. The residue was purified by chromatography (SiO_2, hexane-EtOAc-Et_3N = 80:15:5) to afford the title compound (827 mg, 35%) as yellow crystals. ^1H NMR ($CDCl_3$, 400.13 MHz): δ 1.28 (d, 6H, J = 6.8 Hz); 1.74 (s, 12H); 2.49 (m, 2H); 4.01 (t, 2H, J = 2.3 Hz); 4.06 (m, 2H); 4.08 (m, 2H); 6.87 ~ 6.93 (m, 4H); 6.99 ~ 7.09 (m, 10H); 7.50 (td, 2H, J = 8.1 and 1.1 Hz); 7.53 (td, 2H, J = 6.8 and 1.3 Hz); 7.70 (d, 2H, J = 8.1 Hz); 7.83 (d, 2H, J = 8.1 Hz); 9.16 (t, 2H, J = 7.1 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz): δ –39.47 (s).

Example 41

(R_c, S_{Fe}, S_P)-2,2'-Bis[(α-N,N-dimethylamino)phenylmethyl]-1,1'-bis[(1-naphthyl)phenylphosphino]ferrocene [(R_c, S_{Fe}, S_P)-43]:

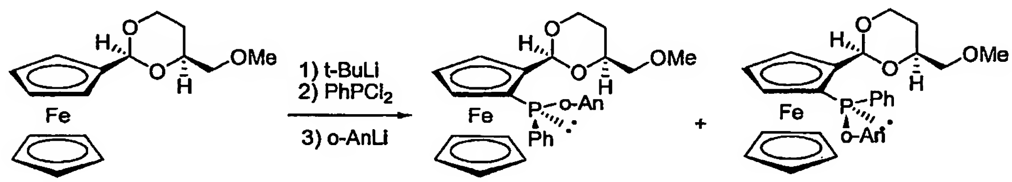


To a solution of (R,R)-1,1'-bis[(α-N,N-dimethylamino)phenylmethyl]ferrocene [(R,R)-23] (903 mg, 2.0 mmol) in Et_2O (20 mL) was added 1.5 M t-BuLi solution in pentane (4.0 mL, 6 mmol) over 10 min via a syringe at –78 °C. After addition was completed, the mixture was warmed to room temperature, and stirred for 1.5 h at room temperature. The resulting red solution was cooled to –78 °C again, and dichlorophenylphosphine (814 uL, 6.0 mmol) was added in one portion. After stirring for 10 min at –78 °C, the mixture was slowly warmed to room temperature, and stirred for 1.5 h at room temperature. The mixture was then cooled to –78 °C again, and a solution of 1-naphthyllithium [prepared from 1-bromonaphthalene (1.45 g, 7 mmol) and 1.5 M t-BuLi solution in pentane (9.3 mL, 14 mmol) in Et_2O (40 mL) at –78 °C] was added slowly via a cannula. The mixture was warmed to room temperature overnight, and filtered through a pad of Celite. The filtrate was concentrated. The residue was purified by chromatography (SiO_2, hexane-EtOAc = 3:1) to afford the title compound (369 mg, 20%) as orange crystals. ^1H NMR ($CDCl_3$, 250.13 MHz): δ 1.54 (s, 12H); 2.46 (m, 2H); 3.01 (m, 2H); 3.96 (t, 2H, J = 2.5 Hz); 4.42 (d, 2H, J = 5.3 Hz); 6.69 (ddd, 2H, J = 7.3, 4.3 and 1.0 Hz); 6.96 ~ 7.34 (m, 22H); 7.55 (d, 2H, J =

8.3 Hz); 7.66 (d, 4H, J = 8.3 Hz); 7.81(d, 2H, J = 7.8 Hz); 9.20 (t, 2H, J = 7.8 Hz); ^{31}P NMR ($CDCl_3$, 162 MHz): δ – 41.73 (s).

Example 42

(2'S, 4'S, S_{Fe}, R_P)-2-[4'-(methoxymethyl-1,3-dioxan-2'-yl]-1-[(2-methoxyphenyl)phenylphosphino]ferrocene [(2'S, 4'S, S_{Fe}, R_P)-46]:



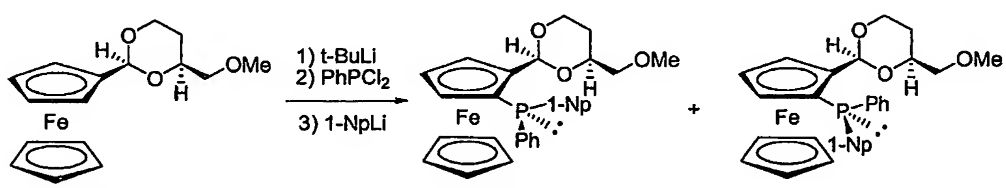
(2S,4S)-45 **(2'S, 4'S, S_{Fe}, R_P)-46**

To a solution of (2S,4S)-4-(methoxymethyl)-2-ferrocenyl-1,3-dioxane [**(2S,4S)-45**] (1.58 g, 5 mmol) in Et_2O (20 mL) was added 1.7 M t-BuLi solution in pentane (3.23 mL, 5.5 mmol) at –40 °C. After stirring for 10 min, the cooling bath was removed and the mixture was warmed to room temperature, and stirred for 1.5 h at room temperature. The resulting orange suspension was cooled to –78 °C, and dichlorophenylphosphine (750 uL, 5.5 mmol) was added in one portion. After stirring for 10 min, the cooling bath was removed and the mixture was warmed to room temperature, and stirred for 1.5 h at room temperature. The mixture was cooled to –78 °C again, a solution of 2-methoxyphenyllithium [prepared from 2-bromoanisole (1.22 mL, 6.5 mmol) and 1.7 M t-BuLi solution in pentane (7.6 mL, 13 mmol) in Et_2O (40 mL) at –78 °C] was added slowly via a cannula. The mixture was warmed to room temperature

overnight, and filtered through a pad of Celite. The filtrate was concentrated. The residue was purified by chromatography (SiO_2, hexane-EtOAc = 6:1) to afford the title compound (2.41 g, 91%) as a mixture of two diastereomers (in about 3.3:1 ratio). Recrystallising from hexane, the major product [(2'S, 4'S, S_{Fe}, R_P)-**46**] (1.41 g, 53%) was obtained. The absolute configuration of (2'S, 4'S, S_{Fe}, R_P)-**46** was determined by single-crystal X-ray diffraction analysis. ^1H NMR ($CDCl_3$, 400.13 MHz): δ 1.42 (dm, 1H, J = 13.3 Hz); 1.74 (m, 1H,); 2.89 (d, 2H, J = 5.1 Hz); 3.03 (s, 3H); 3.59 (m, 1H); 3.60 (s, 3H); 3.74 (m, 1H); 3.91 (td, 1H, J = 12.2 and 2.5 Hz); 4.08 (s, 5H); 4.24 ~4.27 (m, 2H); 4.70 (m, 1H); 5.71 (d, 1H, J = 2.5 Hz); 6.74 (dd, 1H, J = 7.9 and 4.6 Hz); 6.80 ~ 6.86 (m, 2H); 7.22 (m, 1H); 7.31 ~ 7.35 (m, 3H); 7.51 ~7.56 (m, 2H). ^{31}P NMR ($CDCl_3$, 162 MHz): δ –31.46 (s).

Example 43

(2'S, 4'S, S_{Fe}, R_P)-2-[4'-(methoxymethyl-1,3-dioxan-2'-yl]-1-[(1-naphthyl)phenylphosphino]ferrocene [(2'S, 4'S, S_{Fe}, R_P)-47]:



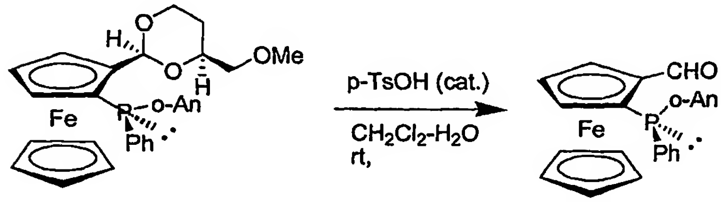
(2S,4S)-45 **(2'S, 4'S, S_{Fe}, R_P)-47**

To a solution of (2S,4S)-4-(methoxymethyl)-2-ferrocenyl-1,3-dioxane [**(2S,4S)-45**] (3.16 g, 10 mmol) in Et_2O (40 mL) was added 1.5 M t-BuLi solution in

pentane (7.4 mL, 11 mmol) at –40 °C. After stirring for 10 min, the cooling bath was removed and the mixture was warmed to room temperature, and stirred for 1.5 h at room temperature. The resulting orange suspension was cooled to –78 °C, and dichlorophenylphosphine (1.49 mL, 11 mmol) was added in one portion. After stirring for 10 min, the cooling bath was removed and the mixture was warmed to room temperature, and stirred for 1.5 h at room temperature. The mixture was cooled to –78 °C again, a solution of 1-naphthyllithium [prepared from 1-bromonaphthalene (1.67 mL, 12 mmol) and 1.5 M t-BuLi solution in pentane (16 mL, 24 mmol) in Et_2O (60 mL) at –78 °C] was added slowly via a cannula. The mixture was warmed to room temperature overnight, and filtered through a pad of Celite. The filtrate was concentrated. The residue was purified by chromatography (SiO_2, hexane-EtOAc = 6:1) to afford the title compound (4.95 g, 90%) as a mixture of two diastereomers (in about 3.4:1 ratio), which was recrystallised from hexane to give the pure major product [(2'S, 4'S, S_{Fe}, R_P)-**47**] (2.53 g, 51%) as yellow needles. The absolute configuration of (2'S, 4'S, S_{Fe}, R_P)-**47** was determined by single-crystal X-ray diffraction analysis. ^{1}H NMR ($CDCl_3$, 400.13 MHz): δ 1.33 (dm, 1H, *J* = 13.3 Hz); 1.63 (m, 1H); 2.56 (dd, 1H, *J* = 10.3 and 4.8 Hz); 2.67 (dd, 1H, *J* = 10.3 and 5.6 Hz); 2.76 (s, 3H); 3.58 (m, 1H); 3.67 (m, 1H); 3.86 (td, 1H, *J* = 12.2 and 2.5 Hz); 4.15 (s, 5H); 3.74 (m, 1H); 4.21 (ddd, 1H, *J* = 11.4, 5.1 and 1.0 Hz); 4.31 (t, 1H, *J* = 2.5 Hz); 4.74 (m, 1H); 5.69 (d, 1H, *J* = 2.5 Hz); 7.16 (ddd, 1H, *J* = 7.1, 5.1 and 1.2 Hz); 7.29 ~ 7.40 (m, 6H); 7.54 ~ 7.58 (m, 2H); 7.74 (d, 1H, *J* = 8.3 Hz); 7.78 (d, 1H, *J* = 8.0 Hz); 8.25 ~8.28 (m, 1H). ^{31}P NMR ($CDCl_3$, 162 MHz): δ – 28.03 (s).

Example 44

(S_{Fe}, R_P)-2-[(2-Methoxyphenyl)phenylphosphino]ferrocenecarboxaldehyde [(S_{Fe}, R_P)-48]:

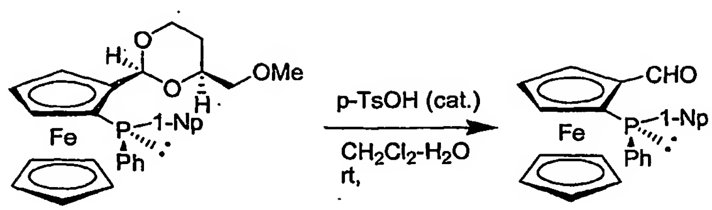


(2'S, 4'S, S_{Fe}, R_P)-46 **(S_{Fe}, R_P)-48**

A mixture of acetal [(2'S, 4'S, S_{Fe}, R_P)-**46**] (4.0 g, 7.5 mmol), p-TsOH.H2O (2.0 g), CH2Cl2 (50 mL) and H2O (30 mL) was stirred for 24 h at room temperature. The organic layer was separated, washed with saturated NaHCO3 solution (20 mL), dried (MgSO4), and evaporated under reduced pressure to give the crude product (3.20 g, 100%) as red crystals, which was used directly in next step. ^{1}H NMR ($CDCl_3$, 250.13 MHz): δ 3.66 (s, 3H); 3.96 (m, 1H); 4.22 (s, 5H); 4.71 (t, 1H, J = 2.3Hz); 5.13 (m, 1H); 6.72 (m, 1H); 6.78 ~ 6.87 (m, 2H); 7.29 (m, 1H); 7.41 (m, 3H); 7.54 (m, 2H); 10.24 (d, 1H, J = 3.3 Hz). ^{31}P NMR ($CDCl_3$, 101 MHz): δ – 34.66 (s).

Example 45

(S_{Fe}, R_P)-2-[(1-Naphthyl)phenylphosphino]ferrocenecarboxaldehyde [(S_{Fe}, R_P)-49]:

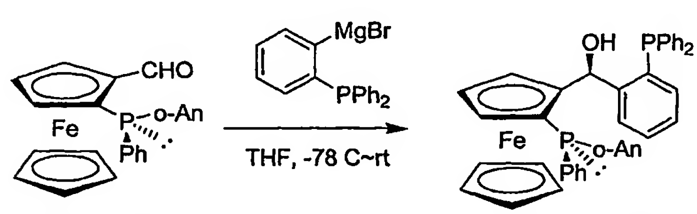


(2'S, 4'S, S_{Fe}, R_P)-47 (S_{Fe}, R_P)-49

A mixture of acetal [(2'S, 4'S, S_{Fe}, R_P)-**46**] (4.73 g, 7.5 mmol), p-TsOH.H_2O (2.0 g), CH_2Cl_2 (50 mL) and H_2O (30 mL) was stirred for 24 h at room temperature. The organic layer was separated, washed with saturated $NaHCO_3$ solution (20 mL), dried ($MgSO_4$), and evaporated under reduced pressure to give the crude product (3.36 g, 100%) as red crystals, which was used directly in next step. ^{1}H NMR ($CDCl_3$, 250.13 MHz): δ 4.04 (m, 1H); 4.28 (s, 5H); 4.76 (t, 1H, J = 2.3Hz); 5.17 (m, 1H); 7.02 (m, 1H); 7.29 ~ 7.48 (m, 6H); 7.52~7.59 (m, 2H); 7.80 (t, 2H, J = 7.5 Hz); 8.26 (m, 1H); 10.20 (d, 1H, J = 3.0 Hz). ^{31}P NMR ($CDCl_3$, 101 MHz): δ – 30.50 (s).

Example 46

(S_{Fe},R_P,αS)-2-[(2-Methoxyphenyl)phenylphosphino]-1-[(diphenylphosphinophenyl)]ferrocenemethanol [(S_P,αS)-51]:



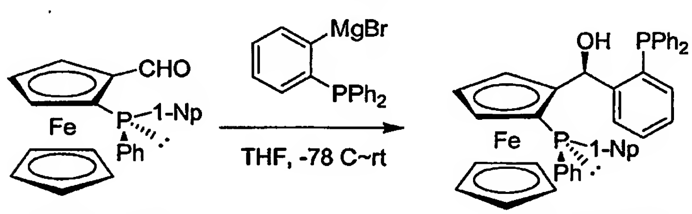
(S_{Fe}, R_P)-48 (S_{Fe}, R_p,αS)-51

A suspension of magnesium turnings (63 mg, 2.6 mmol) and 2-bromophenyl)diphenylphosphine **50** (887 mg, 2.6 mmol) in THF (10 mL) was

refluxed until magnesium was dissolved (about 30 min). The resulting Gragnard reagent solution was cooled to -78 °C, and a solution of (S_{Fe}, R_P)-2-[(2-methoxyphenyl)phenylphosphino]ferrocenecarbaoxaldehyde [(S_{Fe}, R_P)-**48**] (856 mg, 2.0 mmol) in THF (10 mL) was added slowly via a syringe. After stirring for 5 h at -78 °C, the mixture was allowed to warm to room temperature and stirred overnight at room temperature. The reaction was quenched with saturated NH_4Cl solution, and extracted with CH_2Cl_2 (2×20 mL). The combined extracts were washed with brine (20 mL), dried (MgSO4), and evaporated under reduced pressure. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc = 6:1) to give yellow crystals (1.297 g, 96%) as a mixture of two diastereomers (~9:1). Major product: ^1H NMR ($CDCl_3$, 250 MHz): δ 2.91 (br. s, 1H), 3.57 (m, 1H), 3.59 (s, 3H), 4.05 (m, 1H), 4.14 (t, 1H, J = 2.4 Hz), 4.18(s, 5H), 4.22 (m, 1H), 6.48~4.56 (m, 2H), 6.68~6.80 (m, 2H), 7.02 ~ 7.37 (m, 13H); 7.49~7.58 (m, 2H), 7.67 (m, 1H). ^{31}P NMR ($CDCl_3$, 101 MHz): δ -18.69 (d, J = 14.6 Hz), -32.85 (d, J = 14.6 Hz).

Example 47

(S_{Fe},R_P,αS)-2-[(1-Naphthyl)phenylphosphino]-1-[α-[(diphenylphosphinophenyl)]ferrocenemethanol [(S_{Fe},R_P,αS)-52]:

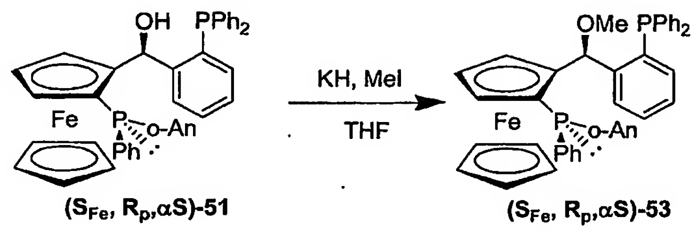


(S_{Fe}, R_P)-49 **(S_{Fe}, R_p,αS)-52**

A suspension of magnesium turnings (63 mg, 2.6 mmol) and 2-bromophenyl)diphenylphosphine **50** (887 mg, 2.6 mmol) in THF (10 mL) was refluxed until magnesium was dissolved (about 30 min). The resulting Gragnard reagent solution was cooled to -78 °C, and a solution of (S_{Fe}, R_P)-2-[(1-naphthyl)phenylphosphino]ferrocenecarbaoxaldehyde [(S_{Fe}, R_P)-**49**] (897 mg, 2.0 mmol) in THF (10 mL) was added slowly via a syringe. After stirring for 5 h at -78 °C, the mixture was allowed to warm to room temperature and stirred overnight at room temperature. The reaction was quenched with saturated NH_4Cl solution, and extracted with CH_2Cl_2 (2×20 mL). The combined extracts were washed with brine (20 mL), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc = 6:1) to give yellow crystals (1.322 g, 93%) as a mixture of two diastereomers (~9:1). Major product: ^{1}H NMR ($CDCl_3$, 250 MHz): δ 2.39 (br. s, 1H), 3.66 (m, 1H), 4.24(s, 5H), 4.29 (t, 1H, J = 2.4 Hz), 4.57 (m, 1H), 4.22 (m, 2H), 6.40~4.49(m, 3H), 6.61~6.67 (m, 2H), 6.83 ~ 7.01 (m, 4H); 7.10~7.59 (m, H), 7.75 (br. D, 1H, J = 7.8 Hz), 8.28 (m, 1H). ^{31}P NMR ($CDCl_3$, 101 MHz): δ -18.54 (d, J = 21.0 Hz), -29.56 (d, J = 21.0 Hz).

Example 48

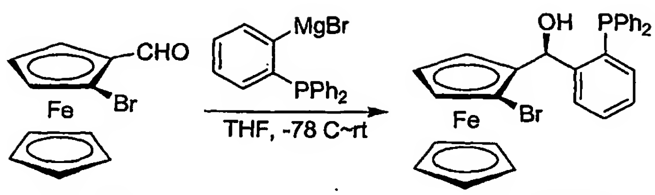
(S_{Fe},R_P,αS)-2-[(2-Methoxyphenyl)phenylphosphino]-1-[α-methoxy-(2-diphenylphosphinophenylmethyl)]ferrocene [(S_{Fe},R_P,αS)-53]:



To a suspension of KH (30%, 174 mg, 1.3 mmol washed with hexane) in THF (10 mL) was added alcohol **[(S_P,αS)-51]** (690 g, 1.0 mmol) at 0 °C. After stirring for 2 h at 0 °C, iodomethane (68 uL, 1.1 mmoL) was added via a syringe, then the mixture was stirred for 2 h at 0 °C. The reaction was quenched with MeOH (0.5 mL), and the solvents were removed under reduced pressure. The residue was dissolved in CH_2Cl_2 (20 mL), washed with water (10 mL) and brine (10 mL), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc = 10:1) to give yellow crystals (463 mg, 66%). ^{1}H NMR ($CDCl_3$, 250 MHz): δ 2.82 (s, 3H), 3.50 (m, 1H), 3.57 (s, 3H), 4.11 (t, 1H, J = 2.3 Hz), 4.17 (s, 5H), 4.19 (m, 1H), 5.79 (d, 1H, J = 6.8 Hz), 6.54~6.64 (m, 2H), 6.69 (m, 1H), 6.84 (ddd, 1H, J =7.8, 4.3 and 1.5 Hz), 7.02~7.37 (m, 12H), 7.52 (m, 2H), 7.66 (m, 1H); ^{31}P NMR ($CDCl_3$, 101 MHz): δ -18.44 (d, J = 18.7 Hz), -31.19 (d, J = 18.7 Hz).

Example 49

(S_{Fe},αS)-2-Bromo-1-[α-(2-diphenylphosphinophenyl)]ferrocenemethanol [(S_{Fe},αS)-55]:

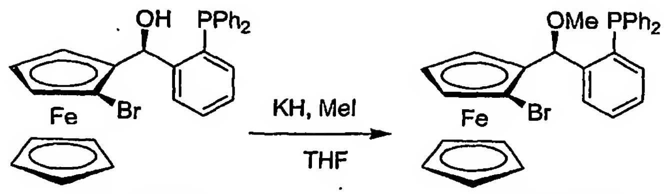


(S_{Fe})-54 (S_{Fe},αS)-55

A suspension of Mg (729 mg, 30 mmol) in THF (10 mL) was added dropwise a solution of 2-bromophenyldiphenylphosphine (**50**) (9.42 g, 27.6 mmol) in THF (30 mL) at about 50 °C. After addition, the mixture was refluxed for 1 h, cooled room temperature, and added to a solution of (S_{Fe})-2-bromoferrocenecarboxaldehyde [(S_{Fe})-**54**](6.74 g, 23 mmol) in Et_2O (20 mL) at -78 °C. After stirring for 6 h at -78 °C, the mixture was warmed to room temperature, and stirred overnight at room temperature. The reaction was quenched with saturated NH_4Cl solution (50 mL), and diluted with EtOAc (100 mL). The organic layer was separated, washed with brine (50 mL), dried (Na_2SO_4), and evaporated under reduced pressure. The residue was purified by chromatography (SiO_2, hexane-EtOAc = 5:1) to give yellow crystals (12.51 g, 98%) as a single diastereomer. ^1H NMR ($CDCl_3$, 250 MHz): δ 2.67 (dd, 1H, J = 3.5 and 2.0 Hz), 4.04 (t, 1H, J = 2.5 Hz), 4.18 (m, 1H), 4.27 (s, 5H), 4.40 (m, 1H), 6.47 (dd, 1H, J = 6.5 and 3.5 Hz), 7.00 (m, 1H), 7.18 (m, 1H), 7.15 ~ 7.37 (m, 12H); ^{31}P NMR ($CDCl_3$, 101 MHz): δ -17.30.

Example 50

(S_{Fe},αS)-2-Bromo-1-[α-methoxy-(2-diphenylphosphinophenylmethyl)]ferrocene [(S_{Fe},αS)-56]:

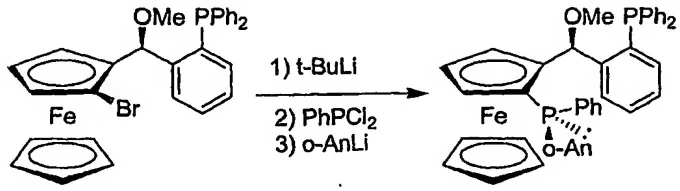


(S_{Fe},αS)-55 (S_{Fe},αS)-56

To a suspension of KH (30%, 3.75 g, 28.1 mmol), washed with hexane) in THF (20 mL) was added a solution of (S_P,αS)-2-Bromo-1-[α-(2-diphenylphosphinophenyl)]ferrocenemethanol **[(S_{Fe},αS)-55]** (12.00 g, 21.6 mmol) in THF (180 mL) at 0 °C. After stirring for 2 h at 0 °C, iodomethane (1.48 mL, 23.8 mmoL) was added via a syringe, then the mixture was stirred for 1 h at 0 °C. The reaction was quenched with MeOH (5 mL), and the solvents were removed under reduced pressure. The residue was dissolved in EtOAc (150 mL), washed with water (100 mL) and brine (10o mL), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc = 5:1) to give yellow crystals (12.10 g, 98%). ^{1}H NMR ($CDCl_3$, 250 MHz): δ 3.29 (s, 3H), 3.96 (t, 1H, J = 2.5 Hz), 4.01 (m, 1H), 4.27 (s, 5H), 4.33 (m, 1H), 6.09 (d, 1H, J = 7.8 Hz), 7.04 (m, 1H), 7.15 ~ 7.37 (m, 12H), 7.44 (m, 1H); ^{31}P NMR ($CDCl_3$, 101 MHz): δ -18.46.

Example 51

(S_{Fe},S_P,αS)-2-[(2-Methoxyphenyl)phenylphosphino]-1-[α-methoxy-(2-diphenylphosphinophenylmethyl)]ferrocene [(S_{Fe},S_P,αS)-57]:

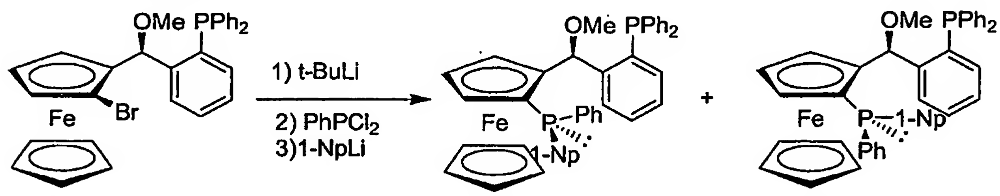


$(S_{Fe},S_P, \alpha S)$**-56** $(S_{Fe},SP, \alpha S)$**-56**

To a solution of bromide **[$(S_{Fe},\alpha S)$-56]** (2.85 g, 5 mmol) in THF (30 mL) was added slowly 1.7 M t-BuLi (6.5 mL, 11 mmol) via a syringe at -78 °C. After stirring for 10 min at -78 °C, $PhPCl_2$ (746 uL, 5.5 mmoL) was added via a syringe, After stirring for 30 min at -78 °C, the mixture was warmed to room temperature and stirred for 1 h at room temperature. the mixture was cooled to -78 °C again, and a suspension of o-AnLi [prepared from 2-bromoanisole (805 uL, 6.5 mmol) and 1.7 M t-BuLi (7.6 mL, 13 mmol) in Et_2O (30 mL) at -78 °C] was added via a cannula, then the mixture was stirred overnight at -78 °C to room temperature. The reaction was quenched with water (20 mL), The organic layer was separated, washed with brine (30 mL), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc = 10:1) to give yellow crystals (3.21 g, 91%) as a single diastereomer. ^1H NMR ($CDCl_3$, 250 MHz): δ 2.71 (s, 3H), 3.67 (m, 1H), 3.90 (m, 1H), 3.96 (s, 3H), 4.06 (t, 1H, J = 2.3 Hz), 4.22 (s, 5H), 5.52 (d, 1H, J = 6.5 Hz), 6.80~6.98 (m, 4H), 7.08~7.36 (m, 14H), 7.76 (m, 1H); ^{31}P NMR ($CDCl_3$, 101 MHz): δ -17.98 (d, J = 10.0 Hz), -33.15 (d, J = 10.0 Hz).

Example 52

(S_{Fe},S_P,αS)-2-[(1-Naphthyl)phenylphosphino]-1-[α-methoxy-(2-diphenylphosphinophenylmethyl)]ferrocene [(S_{Fe},S_P,αS)-58] and (S_{Fe},R_P,αS)-2-[(1-Naphthyl)phenylphosphino]-1-[α-methoxy-(2-diphenylphosphinophenylmethyl)]ferrocene [(S_{Fe},R_P,αS)-59]:



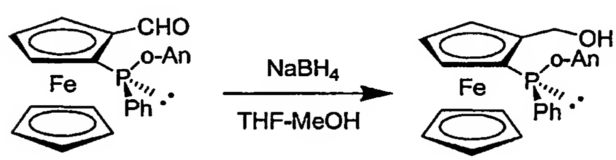
(S_{Fe},S_P, αS)-56 (S_{Fe},S_P, αS)-58 (S_{Fe},RP, αS)-59

To a solution of bromide **[(S_{Fe},αS)-56]** (2.85 g, 5 mmol) in THF (30 mL) was added slowly 1.7 M t-BuLi (6.5 mL, 11 mmol) via a syringe at -78 °C. After stirring for 10 min at -78 °C, $PhPCl_2$ (746 uL, 5.5 mmoL) was added via a syringe, After stirring for 30 min at -78 °C, the mixture was warmed to room temperature and stirred for 1 h at room temperature. Tthe mixture was cooled to -78 °C again, and a suspension of o-AnLi [prepared from 1-bromonaphthalene (900 uL, 6.5 mmol) and 1.7 M t-BuLi (7.6 mL, 13 mmol) in Et_2O (30 mL) at -78 °C] was added via a cannula, then the mixture was stirred overnight at -78 °C to room temperature. The reaction was quenched with water (20 mL), The organic layer was separated, washed with brine (30 mL), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was purified by flash chromatography (SiO_2, hexane-EtOAc = 10:1) to give yellow crystals (3.30 g, 91%) as a mixture of two diastereomers (ratio: ~9:1), which was recrystallised from hexane to give pure major product **[(S_{Fe},S_P,αS)-58]** (2.83 g, 78%) as yellow crystals. The mother liquor was concentrated, and the residue was

recrystallized from MeOH to afford pure minor product **[(S_{Fe},R_P,αS)-59]** (217 mg, 6%) as yellow crystals. Major product **[(S_{Fe},S_P,αS)-58]** : ^{1}H NMR ($CDCl_3$, 250 MHz): δ 2.96 (s, 3H), 3.74 (m, 1H), 3.84 (s, 5H), 4.13 (t, 1H, J = 2.5 Hz), 4.20 (m, 1H), 6.04 (d, 1H, J = 7.3 Hz), 6.89~7.41 (m, 20H), 7.55 (ddd, 1H, J = 8.0, 6.8 and 1.3 Hz), 7.64 (dd, 1H, J = 6.8 and 1.5 Hz), 7.69 (ddd, 1H, J = 5.3, 3.5 and 1.7 Hz), 7.89 (t, 2H, J = 8.0 Hz), 9.32 (dd, 1H, J = 7.5 and 6.8 Hz). ^{31}P NMR ($CDCl_3$, 101 MHz): δ -18.83 (d, J = 21.3 Hz), -35.08 (d, J = 21.3 Hz). Minor product **[(S_{Fe},R_P,αS)-59]:** ^{1}H NMR ($CDCl_3$, 250 MHz): δ 2.73 (s, 3H), 3.61 (m, 1H), 4.21 (t, 1H, J = 2.5 Hz), 4.22 (s, 5H), 4.28 (m, 1H), 5.86 (d, 1H, J = 7.3 Hz), 6.67 (ddd, 1H, J = 7.8, 4.3 and 1.3 Hz), 6.79~7.61 (m, 23H), 7.75 (br. d, 1H, J = 8.0 Hz), 8.29 (m, 1H). ^{31}P NMR ($CDCl_3$, 101 MHz): δ -18.52 (d, J = 18.4 Hz), -27.69 (d, J = 18.4 Hz).

Example 53

(S_{Fe}, R_P)-2-[(2-Methoxyphenyl)phenylphosphino]ferrocenemethanol [(S_{Fe}, R_P)-60]:



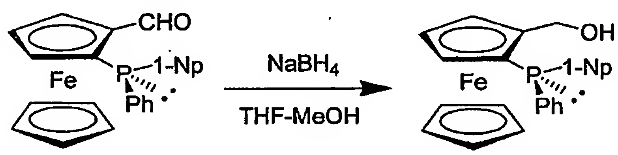
(S_{Fe}, R_P)-48 **(S_{Fe}, R_P)-60**

To a solution of aldehyde [(S_{Fe}, R_P)-**48**] (856 mg, 2.0 mmol) in THF (10 mL) was added $NaBH_4$ (38 mg, 1.0 mmol) at 0 °C, then MeOH (2 mL) was added. After stirring for 2 h at 0 °C, the mixture was warmed to room temperature and stirred overnight at room temperature. The reaction was quenched with saturated

NH_4Cl solution (5 mL), and diluted with EtOAc (10 mL). The organic layer was separated, washed with brine (10 mL), dried ($MgSO_4$), and evaporated under reduced pressure to give the crude product (857 mg, 100%) as yellow crystals, which was used directly in next step. ^1H NMR ($CDCl_3$, 250 MHz): δ 3.63 (m, 1H), 3.66 (s, 3H), 4.10 (s, 5H), 4.29 (t, 1H, J = 2.0 Hz), 4.41 (d, 1H, J = 12.5 Hz), 4.53 (m, 1H), 4.58 (dd, 1H, J = 12.5 and 2.0 Hz), 6.77~6.90 (m, 3H), 7.28 (m, 1H), 7.34~7.41 (m, 3H), 7.48~7.55 (m, 2H). ^{31}P NMR ($CDCl_3$, 101 MHz): δ -35.05.

Example 54

(S_{Fe}, R_P)-2-[(1-Naphthyl)phenylphosphino] ferrocenemethanol [(S_{Fe}, R_P)-61]:



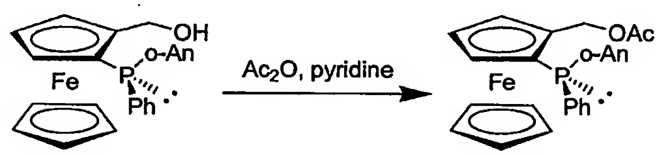
(S_{Fe}, R_P)-49 **(S_{Fe}, R_P)-61**

To a solution of aldehyde [(S_{Fe}, R_P)-**49**] (897 mg, 2.0 mmol) in THF (10 mL) was added $NaBH_4$ (38 mg, 1.0 mmol) at 0 °C, then MeOH (2 mL) was added. After stirring for 2 h at 0 °C, the mixture was warmed to room temperature and stirred overnight at room temperature. The reaction was quenched with saturated NH_4Cl solution (5 mL), and diluted with EtOAc (10 mL). The organic layer was separated, washed with brine (10 mL), dried ($MgSO_4$), and evaporated under reduced pressure to give the crude product (900 mg, 100%) as yellow crystals, which was used directly in next step. ^1H NMR ($CDCl_3$, 250 MHz): δ 3.71 (m,

1H), 4.16 (s, 5H), 4.36 (t, 1H, J = 2.5 Hz), 4.41 (d, 1H, J = 12.5 Hz), 4.54 (dd, 1H, J = 12.5 and 1.3 Hz), 4.58 (m, 1H), 7.11 (ddd, 1H, J = 7.0, 4.5 and 1.3 Hz), 7.30~7.57 (m, 8H), 7.80 (m, 2H), 8.26 (m, 1H). ^{31}P NMR ($CDCl_3$, 101 MHz): δ -31.14.

Example 55

(S_{Fe}, R_P)-2-[(2-Methoxyphenyl)phenylphosphino]ferrocenemethanol acetate [(S_{Fe}, R_P)-62]:

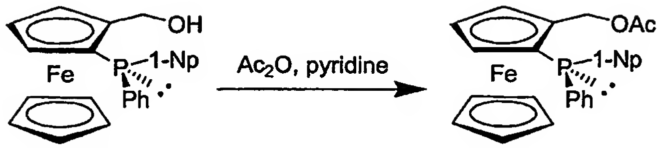


(S_{Fe}, R_P)-60 **(S_{Fe}, R_P)-62**

A solution of alcohol [(S_{Fe}, R_P)-**60**] (857 mg, 2.0 mmol), Ac_2O (2 mL) and pyridine (2 mL) in CH_2Cl_2 (10 mL) was stirred overnight at room temperature. The volatile matters were removed under reduced pressure below 35 °C to give the crude product (880 mg, 100%) as yellow crystals, which was used directly in next step. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.62 (s, 3H), 3.64(s, 4H, overlapped), 4.10 (s, 5H), 4.30 (t, 1H, J = 2.5 Hz), 4.54 (m, 1H), 5.01 (d, 1H, J = 12.0 Hz), 5.12 (dd, 1H, J = 12.0 and 2.3 Hz), 6.77 (m, 2H), 6.83 (t, 1H, J = 7.5 Hz), 7.25 (m, 1H), 7.37 (m, 3H), 7.51 (m, 2H). ^{31}P NMR ($CDCl_3$, 101 MHz): δ -34.60.

Example 56

(S_{Fe}, R_P)-2-[(1-Naphthyl)phenylphosphino]ferrocenemethanol acetate [(S_{Fe}, R_P)-63]:

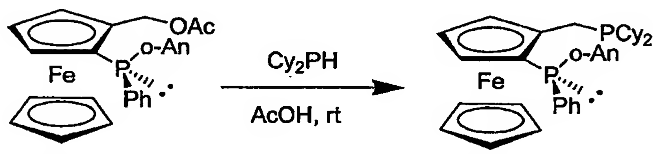


(S_{Fe}, R_P)-61 (S_{Fe}, R_P)-63

A solution of alcohol [(S_{Fe}, R_P)-**61**] (900 mg, 2.0 mmol), Ac_2O (2 mL) and pyridine (2 mL) in CH_2Cl_2 (10 mL) was stirred overnight at room temperature. The volatile matters were removed under reduced pressure below 35 °C to give the crude product (983 mg, 100%) as yellow crystals, which was used directly in next step. ^{1}H NMR ($CDCl_3$, 250 MHz): δ 1.46 (s, 3H), 3.74(m, 1H), 4.15 (s, 5H), 4.38(t, 1H, J = 2.5 Hz), 4.59 (m, 1H), 5.00 (d, 1H, J 1.3.5 Hz), 7.28~7.45 (m, 5H), 7.54 (m, 1H), 7.69 (tt, 1H, J = 7.8 and 1.8 Hz), 7.78 (m, 2H), 8.23 (m, 1H), 8.64 (m, 2H). ^{31}P NMR ($CDCl_3$, 101 MHz): δ -30.85.

Example 57

(S_{Fe}, R_P)-1-[(Dicyclohexylphosphino)methyl]-2-[(2-methoxyphenyl)phenylphosphino]ferrocene [(S_{Fe}, R_P)-64]:



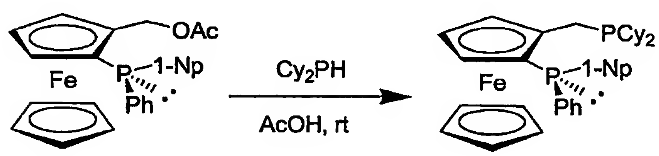
(S_{Fe}, R_P)-62 (S_{Fe}, R_P)-64

A solution of (S_{Fe}, R_P)-**62** (472 mg, 1.0 mmol) and dicyclohexylphosphine (243 uL, 1.2 mmol) in acetic acid (3 mL) was stirred for 7 days at room temperature, and poured into 10% K_2CO_3 aqueous solution (60 mL) with stirring, extracted

with Et_2O (2×25 mL). The combined ether layers were dried ($MgSO_4$) and concentrated. The residue was purified by chromatography (SiO_2, hexane-EtOAc = 9:1) to afford the title compound (573 mg, 94%) as orange crystals. ^1H NMR ($CDCl_3$, 250.13 MHz): δ 0.99~1.79 (m, 22 H), 2.56 (br. d, 1H, J = 12.5 Hz), 2.73 (br. d, 1H, J = 12.5 Hz), 3.58 (m, 1H), 4.00 (s, 5H), 4.20 (m, 1H), 4.57 (m, 1H); 4.32 (m, 1H), 6.74~7.58 (m, 9 H); ^{31}P NMR ($CDCl_3$, 101.25 MHz): δ -2.93; -35.19.

Example 58

(S_{Fe}, R_P)-1-[(Dicyclohexylphosphino)methyl]-2-[(1-naphthyl)phenylphosphino]ferrocene [(S_{Fe}, R_P)-65]:



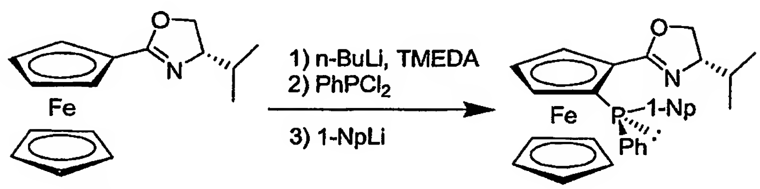
(S_{Fe}, R_P)-63 (S_{Fe}, R_P)-65

A solution of (S_{Fe}, R_P)-**63** (492 mg, 1.0 mmol) and dicyclohexylphosphine (243 uL, 1.2 mmol) in acetic acid (3 mL) was stirred for 7 days at room temperature, and poured into 10% K_2CO_3 aqueous solution (60 mL) with stirring, extracted with Et_2O (2×25 mL). The combined ether layers were dried ($MgSO_4$) and concentrated. The residue was purified by chromatography (SiO_2, hexane-EtOAc = 9:1) to afford the title compound (599 mg, 95%) as orange crystals. ^1H NMR ($CDCl_3$, 250.13 MHz): δ 0.83~1.76(m, 22 H), 2.57 (dm, 1H, J = 12.5 Hz), 2.70 (dm, 1H, J = 12.5 Hz), 3.67 (m, 1H), 4.06 (s, 5H), 4.27 (t, 1H, J = 2.5 Hz),

4.60 (m, 1H); 7.12 (m, 1H), 7.31~7.82 (m, 10 H);8.28 (m, 1H). ^{31}P NMR ($CDCl_3$, 101.25 MHz): δ -2.19; -31.85.

Example 59

(S_C, S_{Fe}, R_P)-67:



(S)-**66** (S_C, S_{Fe}, R_P)-**67**

To a solution of (S)-**66** (1.56 g, 5 mmol) and TMEDA (1.0 mL, 6.5 mmol) in Et_2O (50 mL) was added 2.5 M n-BuLi (2.6 mL, 6.5 mmol) at -78 °C, After stirring for 3 h at -78 °C, $PhPCl_2$ (0.95 mL, 7.0 mmol) was added, After stirring for 20 min at -78 °C, the mixture was warmed to room temperature and stirred for 1.5 h at room temperature. The mixture was cooled to -78 °C again, and a suspension of 1-NpLi [prepared from 1-bromonaphthalene (1.39 mL, 10 mmol) and 1.7 M t-BuLi (11.8 mL, 20 mmol) in Et_2O (40 mL) at -78 °C] was added via a cannula. The mixture was stirred and warmed to room temperature overnight. The reaction was quenched by water (40 mL). The organic layer was separated, washwd with brine (40 mL), dried ($MgSO_4$), and concentrated. The residue was purified by chromatography (SiO_2, EtOAc-hexane = 1:5~1:3) to give the product (2.25 g, 85%) as an orange crystals. ^{1}H NMR and ^{31}P NMR analysis show the de is about 9:1. Major product: ^{1}H NMR ($CDCl_3$, 400.13 MHz): δ 0.58 (d, 3H, J = 6.7 Hz);. 0.73 (d, 3H, J = 6.7 Hz); 1.58 (m, 1H), 3.45 3.52 (m, 2H), 3.61 (m,

1H), 3.78 (m, 1H), 4.29 (s, 5H); 4.44 (t, 1H, *J* = 2.6 Hz); 5.05 (m, 1H); 7.08(dd, 1H, *J* = 7.0 and 4.4 Hz); 7.24 ~ 7.48 (m, 8H); 7.74 (d, 1H, *J* = 8.0 Hz); 7.80 (d, 1H, *J* = 8.0 Hz); 8.37 (dd, 1H, *J* = 8.3 and 4.3 Hz). ^{31}P NMR ($CDCl_3$, 162 MHz): δ – 23.52 (s).

References

1. T. Hayashi, in Ferrocenes, (Eds.: A. Togni, T. Hayashi), VCH, Weinheim, 1995, p. 105.

2. 2. Togni, A.; Breutel, C.; Schnyder, A.; Spindler, F.; Landert, H.; Tijani, A. J. Am. Chem. Soc. 1994, 116, 4062.

3. 3. a. H. U. Blaser,W. Brieden, B. Pugin, F. Spindler, M. Studer, A. Togni, Topics in Catalysis 2002, 19, 3; b. H. U. Blaser, F.Spindler, M. Studer, Applied Catal. A: General 2001, 221, 119.

4. 4. McGarrity, J.; Spindler, F.; Fuchs, R.; Eyer, M. (LONZA AG), EP-A 624587 A2, 1995; Chem. Abstr. 1995, 122, P81369q.

5. 5. a. Blaser, H.-U. Adv. Synth. Catal. 2002, 344, 17. b. Blaser, H.-U.; Buser, H.-P.; Coers, K.; Hanreich, R.; Jalett, H.-P.; Jelsch, E.; Pugin, B.; Schneider, H.-D.; Spindler, F.; Wegmann, A. Chimia 1999, 53, 275.

6. 6. a. N. W. Boaz, S. D. Debenham, E. B. Mackenzie, S. E. Large, Org. Lett. 2002, 4, 2421. b. Boaz, N. W.; Debenham, S. D. US 2002/0065417 (2002)

7. a) T. Ireland, G. Grossheimann, C. Wieser-Jeunesse, P. Knochel, Angew. Chem. Int. Ed. 1999, 38, 3212. b) T. Ireland, K. Tappe, G. Grossheimann, P. Knochel, Chem. Eur. J. 2002, 8, 843;

8. a) M. Lotz, K. Polborn, P. Knochel, Angew. Chem. Int. Ed. 2002, 41, 4708. b) K. Tappe; P. Knochel, Tetrahedron: Asymmetry 2004, 15, 12; c) M. Lotz, P. Knochel, A. Monsees, T. Riermeier, R. Kadyrov, J. J. Almena Perea, Ger. Pat. No. DE 10219490 (Degussa AG).

9. a) T. Sturm, L. Xiao, W. Weissensteiner, Chimia 2001,55, 688; b) W. Weissensteiner, T. Sturm, F. Spindler, Adv. Synth. Catal. 2003, 345, 160; c) Weissensteiner, T. Sturm, F. Spindler, US2003212284.

10. a. Perea, A. J. J.; Borner, A.; Knochel, P. Tetrahedron Lett. 1998, 39, 8073. b. Perea, A. J. J.; Lotz, M.; Knochel, P. Tetrahedron: Asymmetry 1999, 10, 375. c.Lotz, M.; Ireland, T.; Perea, A. J. J.; Knochel, P. Tetrahedron: Asymmetry 1999, 10, 1839. d. Knochel, P.; Perea, A. J. J.; Drauz, K.; Klement, I. US 6,284,925 (2001).

11. (a) Sawamura, M.; Hamashima, H.; Sugawara, M.; Kuwano, N.; Ito, Y. Organometallics 1995, 14, 4549. (b) Sawamura, M.;Kuwano, R.; Ito, Y. J. Am. Chem. Soc. 1995, 117, 9602. (c) Kuwano, R.; Sawamura, M.; Ito, Y. Tetrahedron: Asymmetry 1995, 6, 2521. (d) Kuwano, R.; Okuda, S.; Ito, Y. Tetrahedron: Asymmetry 1998, 9, 2773. (e) Kuwano, R.; Okuda, S.; Ito, Y. J. Org. Chem. 1998, 63, 3499. (f) Kuwano, R.; Ito, Y. J. Org. Chem. 1999, 64, 1232. (g) Kuwano, R.; Sato, K.; Kurokawa, T.; Karube, D.; Ito, Y. J. Am. Chem. Soc. 2000, 122, 7614.

12. a) Kang, J.; Lee, J. H.; Ahn, S. H.; Choi, J. S. Tetrahedron Lett. 1998, 39, 5523. b) Kang, J.; Lee, J. H.; Kim, J. B.; Kim, G. J. Chirality 2000, 12, 378.

13. a) Jendralla, H. ; Paulus, E. Synlett, 1997, 471. b) Jendralla, J. H. US 5,856,540 (1999)

14. a) Argouarch, G.; Samuel, O.; Kagan, H. B. Eur. J. Org. Chem. 2000, 2891. b) Argouarch, G.; Samuel, O.; Riant, O.; Daran, J.-C.; Kagan, H. B. Eur. J. Org. Chem. 2000, 2893.

15. Marinetti, A.; Labrue, F.; Gene^t, J.-P. Synlett 1999, 1975.

16. Berens, U.; Burk, M. J.; Gerlach, A.; Hems, W. Angew. Chem., Int. Ed. Engl. 2000, 39, 1981.

17. You, J.; Drexler, H.-J.; Zhang, S.; Fischer, C.; Heller, D. Angew. Chem., Int. Ed. Engl. 2003, 42, 913.

18. Maienza, F.; Wo¨rle, M.; Steffanut, P.; Mezzetti, A. Organometallics 1999, 18, 1041.

19. (a) Nettekoven, U.; Widhalm, M.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. Tetrahedron: Asymmetry 1997, 8, 3185. (b) Nettekoven, U.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Widhalm, M.; Spek, A. L.; Lutz, M. J. Org. Chem. 1999, 64, 3996.

20. Liu, D.; Li, W.; Zhang, X. Org. Lett. 2002, 4, 4471.

21. Xiao, D.; Zhang, X. Angew. Chem., Int. Ed. Engl. 2001, 40, 3425.

22. a) M. T. Reetz, A. Gosberg, R. Goddard, S.-H. Kyung, Chem. Commun. 1998, 2077; b) M. T. Reetz, A. Gosberg, WO 0014096, 1998 (assigned to Studiengesellschaft Kohle MBH);

23. a. Nettekoven, U.; Widhalm, M.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Mereiter, K.; Lutz, M.; Spek, A. L. Organometallics 2000, 19, 2299. b. Nettekoven, U.; Kamer, P. C. J.; Widhalm, M.; van Leeuwen, P. W. N. M Organometallics 2000, 19, 4596. c. Nettekoven, U.; Widhalm, M.;

Kalchhauser, H.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Lutz, M.; Spek, A. L. J. Org. Chem. 2001, 66, 759-770.

24. Barbaro, P.; Bianchini, C.; Giambastiani, G.; Togni, A. Chem. Commun. 2002, 2672.

25. (a) Marquarding, D.; Klusacek, H.; Gokel, G.; Hoffmann, P.; Ugi, I. J. Am. Chem. Soc. 1970, 92, 5389. (b) Marquarding, D.; Klusacek, H.; Gokel, G.; Hoffmann, P.; Ugi, I. Angew. Chem. Int. Ed. Engl. 1970, 9, 371. (c) Hayashi, T.; Yamamoto, K.; Kumada, M. Tetrahedron Lett. 1974, 15, 405. (d) Hayashi, T.; Mise, T.; Fukushima, M.; Kagotani, M.; Nagashima, N.; Hamada, Y.; Matsumoto, A.; Kawakami, S.; Konishi, M. M.; Yamamoto, K.; Kumada, M. Bull. Chem. Chem. Soc. Jpn. 1980, 53, 1138

26. Riant, O.; Argouarch, G.; Guillaneux, D.; Samuel, O.; Kagan, H. B. J. Org. Chem. 1998, 63, 3511.

27. (a) Riant, O.; Samuel, O.; Flessner, T.; Taudien, S.; Kagan, H. B. J. Org. Chem. 1997, 62, 6733. (b) Riant, O.; Samuel, O.; Kagan,H. B. J. Am. Chem. Soc. 1993, 115, 5835.

28. (a) Richards, J.; Damalidis, T.; Hibbs D. E.; Hursthouse, M. B. Synlett 1995, 74. (b) Sammakai, T.; Latham H. A.; Schaad, D. R. J. Org. Chem. 1995, 60, 10. (c) Nishibayashi, Y.; Uemura, S. Synlett 1995, 79. (d) Sammakai, T.; Latham, H. A. J. Org. Chem. 1995, 60, 6002.

29. Ganter, C.; Wagner, T. Chem. Ber. 1995, 128, 1157.

30. (a) Enders, D.; Peters, R.; Lochtman, R.; Runsink, J. Synlett 1997, 1462. (b) Enders, D.; Peters, R.; Lochtman, R.; Runsink, J. Eur. J. Org. Chem. 2000, 2839.

31. Lotz, M.; Ireland T.; Tappe, K.; Knochel, P. Chirality, 2000, 12, 389.

32. Kitzler, R.; Xiao, L.; Weissensteiner, W. Tetrahedron: Asymmetry 2000, 11, 3459.

33. Widhalm, M.; Mereiter, K.; Bourghida, M. Tetrahedron: Asymmetry 1998, 9, 2983.

34. Nishibayashi, Y.; Arikawa, Y.; Ohe, K.; Uemura, S. J. Org. Chem. 1996, 61, 1172.

35. (a) Tsukazaki, M.; Tinkl, M.; Roglans, A.; Chapell, B. J.; Taylor, N. J.; Snieckus, V. J. Am. Chem. Soc. 1996, 118, 685. (b) Jendralla, H.; Paulus, E. Synlett 1997, 471.

36. Price, D.; Simpkins, N. S. Tetrahedron Lett. 1995, 36, 6135.